JOURNAL

OF THE

INDIAN MEDICAL ASSOCIATION

Vol. XII *Calcutta, December, 1942* No. 3

HEXAMINE AS A URINARY ANTISEPTIC

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The current teaching regarding the action of hexamine is that it liberates formaldehyde in acid urine and that formaldehyde is the real active agent. It is, therefore, worth observing (1) what is the concentration of hexamine and of formaldehyde in urine when administered by mouth (2) is this concentration sufficient by itself to kill or materially inhibit the growth of the infecting organisms?

In this paper* we report the results of experiments to study:—

I. The rate and extent of decomposition of hexamine:

(1) In buffered aqueous solutions, at (*a*) different hydrogen ion concentrations between pH 5·2 and 7, (*b*) different temperatures between 10 and 38°C and (*c*) different initial concentrations of hexamine between 0·22 to 0·88 mol., the other factors in each case being kept constant.

(2) In buffered urine at body temperature and initial concentration of 0·2% at different hydrogen ion concentrations between pH 5·2 and 8.

(3) In unbuffered urine at the same temperature and concentrations as in (2) above but with an initial pH between 5·4 and 6·1.

II. The amount of hexamine excreted unchanged, and the concentration of formaldehyde in urine after oral administration of hexamine in man; and,

III. The antiseptic action of formaldehyde on different organisms in cultures.

METHOD

The method employed for estimating formaldehyde was similar to that of Hanzlik and Collins (1916) with slight changes in detail to suit the conditions of the experiments. For the standardisation of the Congo red which differs a great deal in the intensity and not in the quality of the colour. The longer procedure of Hanzlik was avoided by comparing the various dilutions of Congo red against the colours produced by known dilutions of formaldehyde which was accurately assayed according to the method of the British Pharmacopœia (1932) and the phloroglucin reagent, in 20% caustic soda. The proportions of Congo red and methyl orange which have been worked out for matching the colour developed by different concentrations of formaldehyde are presented in Table I.

Estimation of free hexamine in urine—On a preliminary examination the procedure of distilling the urine with phosphoric or sulphuric acid and estimating the formaldehyde colorimetrically in the distillate was found to be time consuming and fluctuating in result. So, the B.P. 1932 method was applied after standardising

* It is not claimed that this work is absolutely new; we have, however, attempted to obtain more systematic and complete data than we found in the literature available to us.

TABLE I—COMPOSITION OF STANDARD MIXTURES OF CONGO RED METHYL ORANGE (Merck's White Label.)

*Concentration of formaldehyde**		*Dye Solution*			
Proportion	Percentage	c.c.'s Congo red (0·025% in 5% alcohol.)	c.c.'s methyl orange (0·01% in 10% alcohol.)	Distilled water	*Remarks*
1 : 20,000	0·005	17·2	nil	To make 50 c.c.	The quantities of dyes are slightly less than those of Hanzlik and Collins.
1 : 25,000	0·004	12·0	nil		
1 : 30,000	0·0033	8·2	nil		
1 : 40,000	0·0025	7·1	nil		
1 : 50,000	0·002	5·5	nil		
1 : 60,000	0·0016	4·5	nil		
1 : 80,000	0·00125	2·0	0·5		
1 :100,000	0·001	2·0	1·5		

Note—* 1. Liq. formaldehydi (British Drug Houses Ltd.), was used formaking the dilutions, and contained 39·2% W/V formaldehyde. 2. Nessler tubes of 50 c.c. with a column of about 12 cm. are used for comparison.

it with regard to boiling, etc., and the following technic was adopted:

20 c.c. of the freshly passed urine was mixed with 10 c.c. N/I sulphuric acid and boiled gently for half an hour and vigorously for another half an hour until the odour of formaldehyde disappeared. In the meantime 10 c.c. of the same urine were titrated against N/I caustic soda with phenolphthalein as indicator. The boiled sample was cooled and back titrated with N/I caustic soda. From this was deducted the number of c.c.'s of N/I caustic soda of the blank experiment and by multiplying the result with 0·03503, the amount of free hexamine calculated. By this method the result obtained was correct to the extent of 95% in the case of added hexamine.

Deterioration of dilute congo red solutions—On keeping the stock solutions of Congo red and methyl orange exposed to day light for 15 days in colourless bottles it was observed that there was considerable change in the intensity of the colour; hence it is always essential to prepare freshly the stock solution as well as the diluted standard, if possible, once a week.

RATE AND EXTENT OF DECOMPOSITION OF HEXAMINE

I. *Decomposition of hexamine in buffered aqueous solution*—(a) At different pH, the temperature and initial concentration of hexamine being constant:

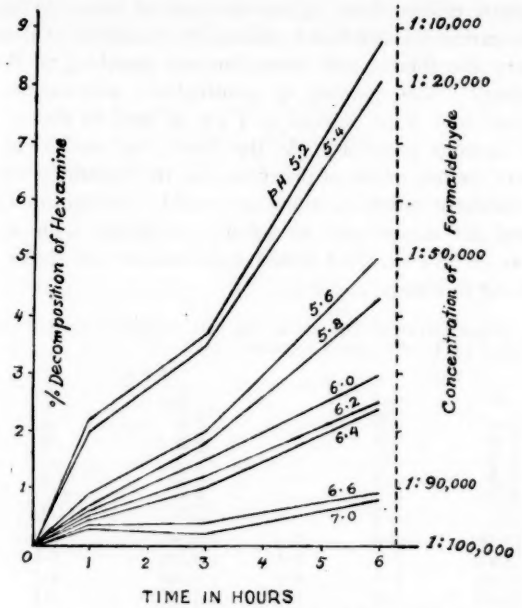
0·2g. hexamine was added to 100 c.c. of buffered mixtures (di-sodium-phosphate and citric acid) in Erlenmayer flasks tightly plugged with cotton, and after incubation in a thermostat at 37° to 38°C, formaldehyde was estimated colorimetrically against freshly prepared standards at regular intervals of time. The time allowed for the maximum development of colour after the addition of the reagent was 1 to 1½ minutes only as the colour begins to fade after this. The percentage decomposition of hexamine was calculated from the amount of formaldehyde estimated.

The results are presented in Table II and Graph 1.

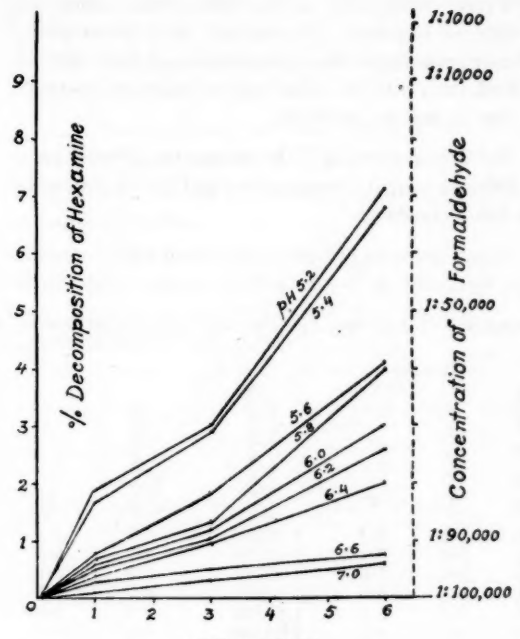
TABLE II—DECOMPOSITION OF HEXAMINE IN BUFFERED AQUEOUS SOLUTION AT DIFFERENT pH—TEMPERATURE 37° TO 38°C, INITIAL CONCENTRATION OF HEXAMINE 0·2%, CONSTANT.

	10 A.M.		11 A.M.		1 P.M.			4 P.M.	
Batch No.	*Initial pH.*	*pH.*	*Concentration of formaldehyde.*	*Total decomposition % of hexamine.*	*pH.*	*Concentration of formaldehyde.*	*Total decomposition % of hexamine.*	*pH.*	*Concentration of formaldehyde.*	*Total decomposition % of hexamine.*
1.	5·2	5·2	1:17,000	2·2	5·2	1:10,000	3·7	5·2	1:7,500	8·8
2.	5·4	5·4	1:18,000	2·0	5·5	1:12,000	3·5	5·4	1:8,000	8·1
3.	5·6	5·6	1:40,000	0·9	5·6	1:18,000	2·8	5·7	1:12,500	5·0
4.	5·8	5·8	1:50,000	0·74	5·9	1:20,000	2·0	5·9	1:15,000	4·3
5.	6·0	6·0	1:55,000	0·68	6·0	1:25,000	1·9	6·0	1:20,500	3·0
6.	6·2	6·2	1:60,000	0·6	6·4	1:28,000	1·5	6·2	1:25,000	2·5
7.	6·4	6·4	1:60,000	0·6	6·4	1:32,500	1·1	6·4	1:27,500	2·4
8.	6·6	6·6	1:80,000	0·46	6·6	1:65,000	0·55	6·6	1:70,000	0·9
9.	7·0	7·0	A trace.	—	7·0	1:80,000	0·4	7·0	—	—
10.	8·0	8·0	nil	—	8·0	—	—	8·0	—	—

The calculations of percentage decomposition are shown after correcting for the quantity used in estimating the pH and formaldehyde—10 c.c. for each estimation.



GRAPH 1—DECOMPOSITION OF HEXAMINE IN BUFFERED WATER



GRAPH 2—DECOMPOSITION OF HEXAMINE IN BUFFERED URINE

It might be mentioned here that Clark's buffer solutions did not suit the purpose as the pH changed in 15 minutes due to their smaller titrable acidity.

(b) At different temperatures, the pH and initial concentration remaining constant.

It is evident from Table III that the minimum temperature below which no decomposition takes place however low the pH be, is 9°C. Any rise in the temperature favours the rate of decomposition.

(c) At different initial concentrations, the pH and temperature remaining constant.

TABLE III—DECOMPOSITION OF HEXAMINE AT DIFFERENT TEMPERATURES,—THE *pH* AND INITIAL CONCENTRATION (0·2%) CONSTANT.

Sample No.	*Initial pH.*	*Total decomposition per cent at the end of 3 hours.*					
		0 to 9° C	10°C.	15°C.	20°C.	30°C.	38°C.
1.	5·2	nil.	0·01	0·05	0·12	2·5	3·7
2.	5·6	nil.	0·006	0·009	0·01	1·8	2·8

Known quantities of hexamine in molecular multiple were added to buffer solutions of different pH and after incubation at room temperature (28° to 30°C) the concentration of formaldehyde was estimated and the percentage decomposition of hexamine calculated (Table IV).

TABLE IV—DECOMPOSITION OF HEXAMINE AT DIFFERENT INITIAL CONCENTRATIONS, pH AND TEMPERATURE REMAINING CONSTANT.

Serial Number	*pH.*	Decompoposition at the end of 2 hours		4 hours.		6 hours.		24 hours.		48 hours.		Initial concentration of hexamine.
		Concentration of formaldehyde	*Total decomposition %*	*Concentration of formaldehyde*	*Total decomposition %*	*Concentration of formaldehyde*	*Total decomposition %*	*Concentration of formaldehyde*	*Total decomposition %*	*Concentration of formaldehyde*	*Total decomposition %*	
1.	6·2	1:80,000	0·4	1:66,000	0·5	1:40,000	1·05	1:30,000	1·3	1:25,000	1·4	0·22 mol.
2.	6·2	1:66,000	0·35	1:50,000	0·3	1:45,000	0·37	1:40,000	0·41	1:18,000	0·91	0·44 mol.
3.	6·2	1:48,000	0·22	1:45,000	0·23	1:40,000	0·26	1:30,000	0·35	1:12,000	0·88	0·88 mol.

From Table IV it is noted that while the quantity of hexamine decomposed in a given period and correspondingly the concentration of formaldehyde attained, rises with the initial concentration of hexamine, the rise is not proportional.

2. *Decomposition of hexamine in buffered urine.* At different pH, the temperature and initial concentration being constant.

Equal volumes of filtered urine and buffer solutions were incubated as before with hexamine, and formaldehyde estimated at regular intervals of time. While comparing the developed colours the standards of dyes were also diluted with urine for easy matching of the colours. The quantity of phloroglucin solution was raised to 1·5 c.c. instead of 1 c.c. as used in the case of aqueous solutions. At the same time we did not filter the precipitate of phosphates as the deposition was sufficiently quick to allow the middle portion to be used for comparison of colours. Filtering with the loss of time involved would make comparison difficult owing to change in colour.

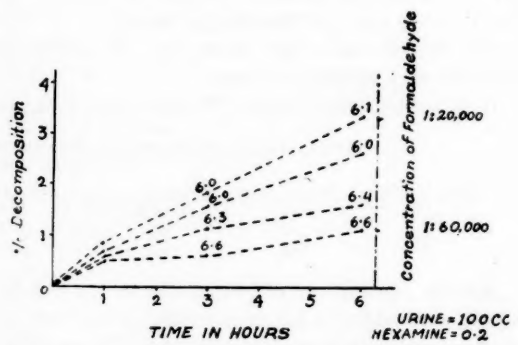
TABLE V. (SEE GRAPH 2.)—DECOMPOSITION OF HEXAMINE IN BUFFERED URINE AT DIFFERENT pH, THE TEMPERATURE (37° TO 38°C) AND INITIAL CONCENTRATION (0·2%) REMAINING CONSTANT.

	10 A.M.		11 A.M.		1 P.M.			4 P.M.		
Serial Number	*Initial pH.*	*pH*	*Concentration of formaldehyde*	*Total decomposition %*	*pH*	*Concentration of formaldehyde*	*Total decomposition %*	*pH*	*Concentration of formaldehyde*	*Total decomposition %*
1.	5·2	5·2	1:20,000	1·9	5·2	1:13,000	3·0	5·2	1:6,500	7·1
2.	5·4	5·4	1:22,500	1·7	5·4	1:15,000	2·9	5·4	1:7,500	6·8
3.	5·6	5·6	1:45,000	0·8	5·6	1:25,000	1·8	5·6	1:9,000	4·5
4.	5·8	5·8	1:52,000	0·7	5·8	1:30,000	1·37	5·8	1:12,000	4·1
5.	6·0	6·0	1:65,000	0·6	6·0	1:32,000	1·3	6·0	1:15,000	3·0
6.	6·2	6·2	1:65,000	0·6	6·2	1:38,000	1·1	6·2	1:17,000	2·8
7.	6·4	6·4	1:65,000	0·6	6·5	1:50,000	0·9	6·4	1:22,000	2·0
8.	6·6	6·6	1:10,0000	0·3	6·6	1:80,000	0·49	6·6	1:45,000	0·8
9.	7·0	7·0	1:10,0000	0·3	7·0	1:10,0000	0·3	7·0	1:10,0000	0·6
10.	8·0	8·0	—	—	8·0	—	—	8·0	—	—

Comparing figures in Table V with those of Table II it will be seen that (1) urinary constituents have some inhibitory effect on the decomposition of hexamine, (2) that there is a sudden fall in the rate of decomposition above pH 5·5.

3. *Decomposition of hexamine in unbuffered urine*—Filtered urines of different pH from different subjects were incubated with hexamine and the results of formaldehyde estimation noted (*vide* Graph. 3).

The point to note in Table VI is that in urine without addition of extra buffer there is a rise of pH during the first few minutes. This is due to the using up of available acid buffer in reacting with hexamine. The rate of liberation of formaldehyde consequently falls.



GRAPH 3—DECOMPOSITION OF HEXAMINE IN UNBUFFERED URINE SHOWING THE CHANGE IN pH

TABLE VI—DECOMPOSITION OF HEXAMINE IN UNBUFFERED URINE AT 37° TO 38°C AND INITIAL CONCENTRATION OF 0·2%

	10 A.M.		11-10 A.M.		1-10 P.M.			4-10 P.M.		
Serial Number	*Initial pH.*	*pH*	*Concentration of formaldehyde*	*Total decomposition %*	*pH*	*Concentration of formaldehyde*	*Total decomposition %*	*pH*	*Concentration of formaldehyde*	*Total decomposition %*
I.	(M) 5·4	5·9	1:60,000	0·8	6·0	1:30,000	1·7	6·1	1:20,000	3·3
II.	(G) 5·6	6·0	1:60,000	0·66	6·0	1:30,000	1·7	6·0	1:25,000	2·6
III.	(B) 5·8	6·0	1:60,000	0·6	6·3	1:45,000	1·1	6·0	1:40,000	1·6
IV.	(N) 6·1	6·2	1:80,000	0·5	6·6	1:80,000	0·63	6·6	1:60,000	1·1

For every 10 c.c. urine 0·5 c.c. reagent was added.

II. Excretion and Concentration of Formaldehyde in the Urine after Oral Administration of Hexamine

Human subjects took hexamine by mouth in, (*a*) single and repeated doses, and (*b*) with acid sodium phosphate and without it.

Undecomposed hexamine was also estimated in the urine. The protocol of the experiment is given below and the results shown in Table VII, from which it will be seen that:

(1) The maximum concentration of formaldehyde in urine attained was 1:29000.

(2) The undecomposed hexamine excreted during the first six hours was 50 to 60% of the total taken.

(3) Subjects varied as regards their rapidity of hexamine excretion.

Subjects: S. W. H. & C. D. N.		Subjects: M. G. M. & E. G.		Subjects: B. D. & T. L.	
7-20 A.M.	Urine collected.	7-20 A.M.	Urine collected.	7-20 A.M.	Urine collected.
7-20 A.M.	1g. acid sodium phosphate in 30 c.c. water.	7-20 A.M.	1g. acid sodium phosphate in 30 c.c. water.	7-20 A.M.	2g. acid sodium phosphate in 30 c.c. water.
7-40 A.M.	1g. hexamine in 30 c.c. water.	7-40 A.M.	1g. hexamine in 30 c.c. water.	7-40 A.M.	2g. hexamine in 30 c.c. water.
8-40 A.M.	Urine collected.	8-40 A.M.	Urine collected.	8-40 A.M.	Urine collected.
9-10 A.M.	A glass of milk.	9-10 A.M.	Bread, butter, coffee & water.	9-10 A.M.	Chapati and potato curry and water.
10-40 A.M.	Urine collected.	10-40 A.M.	Urine collected.	10-40 A.M.	Urine collected.
10-40 A.M.	1g. acid sodium phosphate in 30 c.c. water.	10-40 A.M.	1g. acid sodium phosphate in 30 c.c. water.	10-40 A.M.	30 c.c. water.
11 A.M.	1g. hexamine in 30 c.c. water.	11 A.M.	1g. hexamine in 30 c.c. water.	11 A.M.	30 c.c. water.
1 P.M.	A glassful of water.	1 P.M.	A glassful of water.	1 P.M.	A glassful of water.
1-40 P.M.	Urine collected.	1-40 P.M.	Urine collected.	1-40 P.M.	Urine collected.

Table VII—Free and Decomposed Hexamine in Urine after Oral Administration

Subjects	7-20 A.M. Quantity of urine.	pH	Concentration of formaldehye	8-40 A.M. Quantity of urine.	pH	Concentration of formaldehyde	Undecomposed hexamine	Total decomposition % of hexamine
S. W. H.	25 c.c.	5·4	nil.	90 c.c.	5·2 5·3	1: 55,000	0·12	0·12
C. D. N.	252 c.c.	6·4	nil.	300 c.c.	6·2	Trace.	0·57	
M. G. M.	20 c.c.	5·2	nil.	35 c.c.	5·5	1:100,000	0·2	
E. G.	35 c.c.	5·5	nil.	35 c.c.	5·9	1: 70,000	0·06	
T. L.	90 c.c.	5·4	nil.	35 c.c.	5·5	1: 80,000	0·13	
B. D.	75 c.c.	6·6	nil.	38 c.c.	6·1	1:100,000	0·24	

10-40 P.M. Quantity of urine	pH	Concentration of formaldehyde	Undecomposed hexamine	Total decomposition % of hexamine	1-40 P.M. Quantity of urine	pH	Concentration of formaldehyde	Undecomposed hexamine	2-30 P.M. Quantity of urine	pH	Concentration of formaldehyde	Undecomposed hexamine
							1:29,000					
252 c.c.	5·5	1:40,000	0·39	0·57	96 c.c.	5·5	1:30,000	0·3	60 c.c.	5·9	1:40,000	0·07
160 c.c.	5·9	1:60,000	0·12		252 c.c.	6·1	1:40,000	0·3	252 c.c.	6·2	1:100,000	0·19
320 c.c.	6·1	1:200,000	0·48		280 c.c.	6·1	1:60,000	0·4	90 c.c.		1:70,000	0·19
224 c.c.	6·1	1:100,000	0·4		244 c.c.	6·0	1:60,000	0·3	104 c.c.	6·0	1:40,000	0·21
175 c.c.												
55 c.c.	6·2	1:40,000	0·42		52 c.c.	6·6	Trace.	0·42	182 c.c.	7·0	Trace.	0·4
65 c.c.	6·2	1:45,000	0·38		225 c.c.	6·4	1:80,000	0·45	224 c.c.	6·7	Trace.	0·32

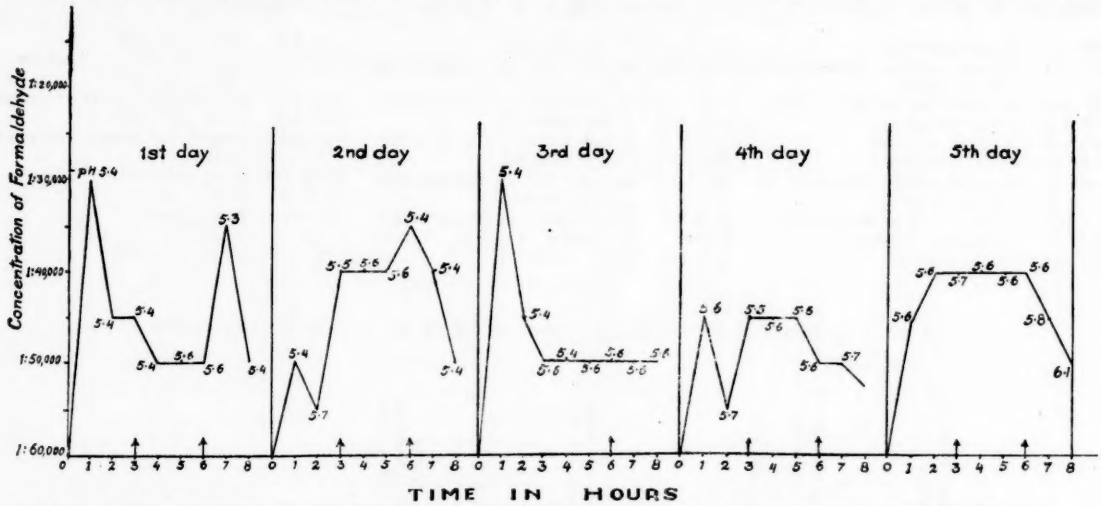
N.B.—In the case of S. W. H., the excretion was followed till 6 A.M. next morning when it was noted that the total excretion of hexamine during this period was about 80%.

Concentration of formaldehyde after repeated administration of hexamine—For this a healthy adult was given 1g. hexamine every 3rd hour for 3 doses preceded by 1g. acid sodium phosphate for five consecutive days and the hourly samples of urine were subjected to formaldehyde estimation. The subject complained of severe burning sensation during micturition from the 2nd day; the acid sodium phosphate was then stopped, and the burning sensation disappeared on the 4th day. The results are represented in Graph 4.

Even in this case the concentration of formaldehyde never rose higher than 1:30,000. The one advantage of repeated administration of hexamine as noted in the experiment was the persistence of the concentration for some hours in spite of a low acidity of urine.

Hexamine and acid phosphate in a mixture—In order to test the advisability of giving the two together in a mixture the following experiment was made.

3g. each, of acid sodium phosphate and hexamine in 100 c.c. water was stocked in a well-stoppered



GRAPH 4—FORMALDEHYDE CONCENTRATION IN URINE AFTER REPEATED ORAL ADMINISTRATION OF HEXAMINE AND ACID SODIUM PHOSPHATE

1·0 gm. Acid Sodium Phosphate in 30 c.c. water at 7-10 a.m. and 1 p.m.
1·0 gm. Hexamine in 30 c.c. water at 7-30 a.m., 10-30 a.m. and 1-30 p.m.
Due to burning sensation during micturition Acid Sodium Phosphate was stopped from the 3rd day, burning disappeared on the 4th day.

colourless bottle and the concentration of formaldehyde estimated every third hour. It was noted that at the end of 9 hours a concentration of 1:13,000 corresponding to 1·92% decomposition of hexamine was attained in the mixture. This is too high for internal use.

III. THE ANTISEPTIC ACTION OF FORMALDEHYDE ON DIFFERENT ORGANISMS IN CULTURE IN VITRO

To study this 0·1 c.c. of broth cultures of *B. typhosus, B. coli, Staphylococcus albus* and *B. proteus* X 19, were added to different concentrations of formaldehyde in nutrient broth at pH 7, incubated at 37°C, and motility in hanging drop preparations (in case of *B. typhosus* and *B. coli*), growth as shown by development of turbidity, and the results of subculture after 24 and 48 hours were noted. Control observations with saline solution instead of broth similarly treated were also made.

The results were as follows:—

(1) *B. typhosus*—while formaldehye 1: 30,000 in saline was sufficient to give negative subcultures, 1: 18,000 in broth could not prevent growth.

(2) *B. coli*—1: 20,000 in saline showed no growth, whereas 1: 10,000 in broth could not prevent it.

(3) *Staphylococcus albus*—1: 20,000 in saline showed no growth while 1: 12,000 broth could not prevent it.

(4) *B. proteus X 19*—1: 10,000 in saline showed no growth, while 1: 5,000 in broth could not prevent it.

On varying the pH of nutrient broth positive subcultures of *B. coli* were obtained with 1:12,000 at pH 7·6 and 1: 16,000 at pH 6·5 and pH 5·5 but not at pH 4·6. Other organisms were not treated in this way.

It is evident that in cultures *in vitro* while a lower pH value itself assists the action of formaldehyde, the minimum effective concentration is in all cases higher than has been obtained in urine in our human subjects after oral administration of hexamine.

Let us review briefly the principles of action of disinfectants and antiseptics, urinary antiseptics in particular, and the different conditions in which they may have to be used, and our aims in using them.

The destruction of pathogenic bacteria outside the body, even in media containing a fair amount of organic matter is a comparatively simple problem and can be solved successfully as two of the important conditions for the action of disinfectants, *viz.*, (1) concentration, and (2) time of exposure, can be satisfied easily and we do not need to take into consideration the inactivation of the germicidal agent, or its removal from the field of action, apart from such portions of it as may enter into combination with the bacterial or other organic matter, which under these conditions is a known and constant quantity. When, however, we consider the destruction of pathogens on or in the animal body, we are faced with various handicaps:—

(1) The drug may be more harmful to the body cells than to the pathogens and unless destruction of the surface cells of the part on which it is used can be disregarded, its use may not be practicable.

(2) The drug may be absorbed in greater or less amount which may suffice to produce systemic poisoning. Even so, application of germicides to surfaces can be made with a fair amount of success. In the case of organisms invading internal organs and the blood stream, a drug given by mouth is liable to undergo changes in the digestive tract and liver, generally of such a nature as to render it inactive; if given intravenously, although its maximum concentration is available for action at once, in most cases foreign substances introduced into the blood tend very rapidly to be put out of the way into the sidings formed by organs such as the liver or are thrown out of the body more quickly.

In dealing with infections of the genito-urinary tract, there is one factor in favour of the action of the drug, provided it has not already been inactivated by the body before its excretion, *viz.*, that during the course of excretion, the kidney concentrates many substances, so that a much higher concentration is present in the urine than in the blood:—

(1) Infections introduced from without at the lower end of the urinary tract as is seen for example in gonorrhœal urethritis, or cystitis in repeated catheterisaton, especially if there is a bladder pouch in which urine stagnates.

While the condition is acute any increase in the acidity of urine is very painful and thus the use of hexamine is rendered impracticable in gonorrhœal urethritis. In the chronic condition, when the organisms have invaded the crypts, glands and ducts opening into the urethra which are not washed by the urine we cannot expcet any action on the organisms lodged there.

The most favourable condition would seem to be that in cystitis, when the antiseptic excreted from each dose can get several hours to act.

(2) Infection of the kidneys either backwards from the lower passages or from the blood as in enteric fever.

Here we must remember that hexamine cannot liberate any formaldehyde in the blood and that the action in the kidney can start only after the tubule is reached, where concentration of acid and hexamine for it to act on, occurs. It may be pointed out that testing the action of hexamine by adding it to urine with the infecting organism outside the body, and incubating it for a number of hours at body temperature does not reproduce the conditions of action within the body.

In the first case, the full quantity of hexamine is present from the beginning and the concentration of formaldehyde is a constantly rising one; in the second, hexamine is only gradually excreted, at first in increasing and then in diminishing quantity (the same may apply to acid) and the concentration of formaldehyde attained gradually at the end of some hours has not much time to act before urine is voided and along with it the formaldehyde is lost from the field of action; the process has to start over again in the case of the next dose.

If we examine the possible aims in using these antiseptics, they can be twofold: (1) To prevent the urine or the patient being a source of infection to others, and (2) to prevent local and general injurious effects of the organisms on the patient himself.

In the case of the urine, at least, disinfection outside the body by means of strong but cheap disinfectants is easily attainable, if desired.

As regards beneficial effects on the patient himself, it is notoriously difficult to assess the value of any form of treatment clinically used; if one may state one's impression (S.W.H) unsupported by large numbers of data and corroboration by cultures, etc.—it would appear that in some cases a continuing high temperature in typhoid is sometimes brought down on instituting hexamine therapy; admitting that the benefit is due to the drug, the data given above do not warrant the conclusion that it could be due to the direct actions of formaldehyde.

Summary and Conclusion

1. The concentration of formaldehyde obtainable in urine after oral administration of hexamine is not sufficient by itself to kill or inhibit the growth of organisms such as *B. typhosus* in the urinary tract.

2. Any beneficial effect of hexamine therapy must, therefore, be atttributed to the liberated formaldehyde acting as a reinforcement to the protective mechanisms of the body already in operation.

3. As an alternative, one may question altogether the efficacy of formaldehyde and attribute the benefit to the hexamine itself, acting in some way hitherto not understood, as in the case of many other chemotherapeutic agents. But the proof in favour of its effectiveness in situations where formaldehyde cannot be liberated, *e.g.*, in gall bladder infections and meningitis is still less clear than in typhoid bacilluria.

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THE STEROIDS OF CHOLESTEROL GROUP

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'Chole' meaning bile and 'steros' meaning solid, cholesterol is a solid substance present in bile; but the solid present in bile mainly consists of various bile salts, cholesterol being present in very small amounts. It is only when the bile reservoir (gall bladder) fails to maintain its normal functions that a concretion takes place resulting in the formation of a mass known as gallstone which is frequently composed of cholesterol. Of course, this sterol is present in all cells of the animal organism, in largest amount in the brain tissue, spinal cord, suprarenal glands and in egg yolk. We get it from our diet; but it is also partly formed in the organism. The mechanism of its formation is, however, unknown. The carbohydrates (Vanghelovici, 1934), the fats (Maclaclan, 1936), or the carotene (Bryant, 1935) of the body may give rise to this characteristic sterol. Whatever may be its mode of occurrence the cholesterol (II) is further being etched away and/or being degraded to give rise to bile acids, vitamin D's, sex hormones, cardiac glucosides and similar other biologically important compounds all containing the reduced cyclopenteno-phenanthrene ring(I).

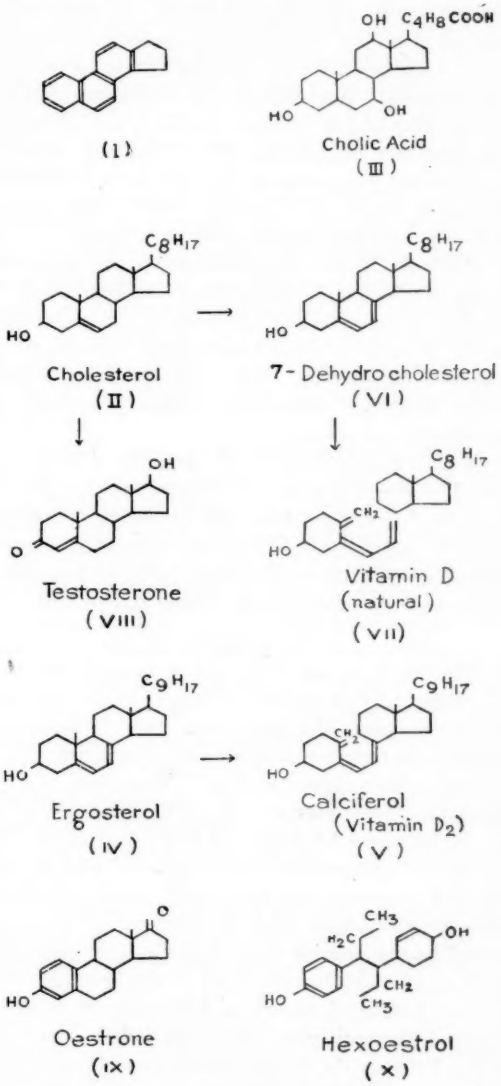
Bile Acids—Human bile is a golden brown viscid liquid having an alkaline reaction. It consists of bile salts chiefly sodium tauroglycocholate, a small amount of cholesterol, lecithin and bile pigments. The bile acids have the property of combining with fatty acids rendering them soluble and/or diffusible in alkaline solution, and thereby, helping in the absorption of fats and lipoids on the intestinal mucosa. They on alkaline hydrolysis give mainly cholic acid (III) which may be further oxidised to dehydrocholic acid, a product largely used in biliary disorders. The relationship with cholesterol group has been established by the synthesis of lithocholic acid—one of the natural bile acids—from cholesterol itself.

Vitamin D—It is now known that calciferol (V) (vitamin D_2) may be obtained by the irradiation of ergosterol (IV). The antirachitic effect of this vitamin when tested on chicks is found to be less than that present in cod liver oil. The 22-dihydro-ergosterol on irradiation, however, gives a more active product.

These observations led to a similar study on the influence of the ultraviolet rays in the molecular or structural alterations in cholesterol ring. The result is the isolation of the vitamin D_3 (VII) as found in tunny liver oil by irradiation of 7-dehydrocholesterol (VI). The antirachitic activity of natural vitamin and that of vitamin D_3 are of the same order whether tested by rat or chick method. In fact any sterol containing a conjugated double bonded system as present in ergosterol (IV) or 7-dehydro cholesterol (VI) may be activated by irradiation. The conversion of the body cholesterol to vitamin D like substances when exposed to sunlight rich in ultraviolet rays may also be dependent on the preliminary formation of 7-dehydrocholesterol. Vitamin D, one of the most important biological substances, undoubtedly owes its origin from the characteristic cholesterol molecule.

Sex Hormones—Testosterone (VIII) m.p. 154-154·5° is the physiologically active natural hormone that is being secreted by the interstitial cells of the testes. It induces and maintains the male secondary sex characteristics and appears to act by stimulating gonadal activity. Its proprionate is now-a-days being used in cases where there is deficient production of natural male sex hormone. This and the other male hormone, androsterone m.p. 182-183° as found in urine have been successfully synthesised from cholesterol pointing thereby the mystic nature of cholesterol.

Oestrone (IX), m.p. 259° is the female hormone isolated from urine during pregnancy and found to be a good therapeutic agent for the relief of the menopause and other conditions that accompany 'change of life' in women between the ages of 40 and 50 years when ovarian function decreases. It has also been synthesised from ergosterol (Marker *et al*, 1936) showing thereby the existence of a structural relationship between sterol and the sex hormone. As the yield is very poor the investigation is of no practical importance. The systematic investigations in this direction have, however, afforded another simple compound 4:4—dihydroxy-alpha: beta—diethyl stilbene, as a white odourless compound, m.p. 167-171°. It is capable of inducing follicular smears, vaginal cornification and withdrawal bleeding in amenorrhœa and the menopause. It is actively oestrogenic even when given by mouth. The daily dose varies from 0·1 to 5 mgm. A still more potent substitute is again being found in its dihydro deriva tive (X), m.p. 184-185°. It possesses all of the important effects of the natural oestrogenic hormones, namely, promotion of uterine growth, stimulation of vaginal mucosa, growth of breasts, inhibition of lactation, and of the activity of the anterior pituitary gonadotropic and growth hormones.



Corpus Luteum Hormone—Progesterone existing in two forms—one prismatic, m.p. 128°, and another in needles, m.p. 121°, is the active substance of corpus luteum (yellow body) formed following the ripening and rupture of the follicle in the human ovary. This hormone plays an important role in the second half of the

menstrual cycle. After rupture of the follicle and ovulation it maintains favourable conditions in the uterus for the reception of the ovum in the event of fertilization. In case no conception takes place, the corpus luteum degenerates and menstruation occurs. If fertilization of the ovum occurs, the corpus luteum continues to excrete its hormone until its function is taken over later by the placenta. Any deficiency in the excretion of this hormone may lead to various disorders like dysmenorrhœa, toxæmia or habitual and threatened abortion. This hormone, progesterone, has now been synthesised (Butenandt, 1934 and Fernholz, 1938) from another sterol—stigmasterol, isolated from soya bean.

Adrenal Cortex Hormone—Desoxycorticosterone recently obtained (*cf. Chem. Abs.*, 1939, p. 7395) by oxidation of progesterone again with lead tetra-acetate is being detected in the adrenal cortex along with the hormone corticosterone. These are known to regulate the body fluids and maintain the sodium potassium concentration in the system.

Active principles of squill, digitalis and strophanthus—The chemical nature of these physiological active substances has not yet been fully revealed. They are, glucosides and have been found to bear a close biogenic relationship with the sterol group by their degradation to a group of lactones closely related to bile acid.

Conclusion

The work on all these sterol groups and their various degradation products is one of the most spectacular achievements of organic chemistry. Testosterone, androsterone, œstrone, progesterone—the important sex hormones, have been isolated from them in the laboratory. The question naturally arises how are then the hormones being formed in the organism? The physiological observations so far recorded tend to show that these hormones owe their origin to the stimulating action of still another kind of hormone, or, hormones secreted by the anterior lobe of the pituitary gland—the chemistry of which is not known. We, however, know that the cholesterol occurs in largest amounts in the brain and nerve tissues. Does this indicate any relationship between the sterols and hormones? The production of a compound of the type hexoestrol (X) again tends to show that a cyclopentenophenanthrene structure is not essential for the development of the biological activity in any substance. Vitamin D also does not possess this characteristic ring. All these, therefore, demand a more systematic investigation on the origin

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of these interesting physiological bodies. Otherwise, the whole problem of the chemistry of these biological substances remains in mystery.

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NORMAL LEVEL OF TYPHOID AGGLUTININS IN THE UNITED PROVINCES

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In the Widal's agglutination test for typhoid fever when a positive result is obtained the next problem is to decide if the particular titre or the maximum dilution upto which the typhoid suspension is agglutinated indicates infection with typhoid fever. The answer usually depends on (1) the level of normal agglutinins in general population, (2) stage of the disease, and (3) history of previous inoculation or infection.

As the normal level of agglutinins have not been worked out in this part of the country I thought it useful to obtain this information. For this purpose I utilised the sera which are sent for Wassermann's test to the Pathology Department of the King George's Medical College.

I used the suspensions of the following organisms:

1.	B. typhosus (H)	T
2.	B. paratyphosus A (H) ..	A
3.	B. paratyphosus B (H) (type phase)	B
4.	B. Cholera Suis Var. Kunzendorf. (monophasic or Group Suspension H)	G
5.	B. typhosus (O)	O
6.	B. typhosus (Vi)	Vi

Abbreviations used later.

The first four were formolised suspensions of broth cultures (1 c.c. containing 500 million organisms) while the O suspension consisted of a precipitate obtained by mixing a thick saline suspension of B. typhosus and alcohol and resuspended in saline (1 c.c. containing 1000 million organisms.) The agglutinability of these suspensions was the same as that of standard Oxford suspensions. B. typhosus Vi suspension used in this work was obtained from Enteric Laboratory, Kasauli.

The tests were carried out according to Dreyer's technique and the end titre obtained in every case. H suspensions were kept in a water bath at 56°C for 2 hours. O suspensions were kept at 56°C for two hours followed by 37°C for 12 hours. Vi suspensions were kept at 37°C for 12 hours.

The results obtained from 300 sera are as follows:

	4 1:25	4 1:50	1 1:125	1 1:250 or above	10 Total
T	9	6	3	4	22
B	4	3	1	2	10
G	6	2	2	2	12
O	6	2	2	1	11
Vi	1	—	—	—	1
Total	30	17	9	10	66

Analysis of Various Agglutinins

T	.. 16		T A	..	1
A	.. 7		T G	..	1
B	.. 7		T B G	..	1
G	.. 7		A G O	..	1
O	.. 4		A B G	..	1
Vi	.. 1		B O	..	1
TO	.. 4		G O	..	1
	46				7

On analysing these figures, one finds that 18 per cent are likely to show positive result in one or more of the typhoid antigens used in the Widal test. It means that one in six persons giving a positive Widal test (especially in low dilutions) may not be suffering from typhoid fever.

Largest number of positives were obtained in the case of B. typhosus suggesting that it is the most commonly infecting organism. The same frequency is found if both clinically positive and Widal positive cases are analysed. In a series of such 100 cases the following result was obtained:

Infecting organism	*per cent*
B. typhosus	.. 76
B. paratyphosus A	.. 16
B. paratyphosus B	.. 8

The above figures show that persons showing normal agglutinins for B. paratyphosus A are practically equal to those for B. paratyphosus B, while the enteric cases show that the incidence of B. paratyphosus A infection is double that of B. paratyphosus B. It may be due to the fact that B. paratyphosus B produces a subclinical infection leading to the production of agglutinins but no fever. The analysis of various agglutinins shows that 12 cases out of 300 persons showed agglutinins against group flagellar antigens. Of these 7 had agglutinins for group flagellar antigens only, showing that these cases were infected with organisms of typhoid (Salmonella) group not included in the routine Widal test. Vi agglutinins were observed in one case only (0·33 per cent) and should be considered rare in the normal persons.

Two cases were positive for both G and B and, as B. paratyphosus B possesses group flagellar antigens, the presence of G was due to infection by B. paratyphosus B. One case had T agglutinins. It is possible that these two cases must have been infected with some organisms of Salmonella group in addition to B. typhosus and B. paratyphosus A, for group flagellar antigens are absent from B. typhosus and B. paratyphosus A.

In addition to the two cases mentioned above, the analysis shows two other cases of double infections (A B G and T B G). As there is no history of prophylactic inoculation as prophylactic inoculation is rare among the hospital class of patients, and as all the three T. A. B. agglutinins were not present in one case, the above two cases (0·6 per cent) appear to be real cases of double infection and not due to any prophylactic inoculation.

Looking at the O agglutinins we find that 11 sera (about 4 per cent) showed O agglutinins. If O suspension of A and B were also used it is possible that more positives would have been obtained. As there are common minor O antigens in T. A. and B and others which become prominent in human infections the figures obtained with B. typhosus O give a fair idea of the O agglutinins present in the general population.

The analysis shows that in 4 cases only O agglutinins were present. It is possible that only O agglutinins developed in these cases but the view that they were infected with nonmotile strains of typhoid organisms appears to be more likely. Though such cases amount to only about 1 per cent they emphasize the need of always including an O suspension in a Widal test.

Out of the 20 infections with pure B. typhosum we find that only four (5 per cent) showed O agglutinins or taking the 53 cases with positive Widal for any typhoid organism we find 11 out of 54 (about 20 per cent) showing O agglutinins. Though I can not give any exact figures the percentage of O agglutinins in Widal positive patients is of the same order. Of course, it must be realised that O agglutinins are shortlived and they are likely to be present more in clinical cases than in normal population. It is possible that these cases in general population might have recently recovered from some enteric infection, for no histories are

(*Continued at foot of next page, 2nd column*)

HAEMOGLOBINURIA—A SUGGESTED TREATMENT

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The condition is known or detected by the blood pigment in the urine. The pigment is oxyhæmoglobin, methæmoglobin, acid or alkali hæmatin. The urine has a red or brownish red colour, sometimes black, when it is known as black water fever.

Varieties

The following are the varieties of hæmoglobinuria:

1. *Toxic.* (*a*) Overuse of potassium chlorate, pyrogallic acid, carbolic acid, arseniureted hydrogen, carbon monoxide, napthol, and muscarine. (*b*) Poisons of scarlet fever, yellow fever, typhoid fever, malaria and syphilis. (*c*) Severe burns. (*d*) Exposure to excessive cold, violent muscular exertion. (*e*) Epidemic hæmoglobinuria of the newborn.

2. *Paroxysmal.* Rarely fatal; passes off in a day or two; more frequent in males; specially associated with cold; also a complication of Reynaud's disease; comes suddenly after mental or physical exhaustion.

Causes

Presence of a hæmolysin is the exciting cause. Alteration of acid base ratio in the blood or acidosis is the predisposing factor.

Mechanism of Production of Haemoglobinuria

The corpuscles are dissolved, the colouring matter is discharged in the blood. The reticuloendothelial system tackles it. Excessive production of bilirubin leads to bilirubinæmia and hæmolytic jaundice. Excreted in the intestine, the pigments are converted into urobilin which is absorbed in the circulation. If excessive hæmoglobin is set free, the endothelial cells fail to tackle it. Kidneys excrete it. It is excreted as oxyhæmoglobin, methæmoglobin, acid or alkali hæmatin. Kidneys stand the risk of being choked.

Acidosis either due to fever, altered metabolism, preexisting anæmia, accentuating local or general oxygen deficiency, unsaturated fatty acid or lyso-lecithin can bring about an attack. In acidosis, the acid base equilibrium of blood is disturbed; there is diminution of alkali reserve.

The buffer quality of blood is due to the presence in the plasma of phosphates, basic bicarbonates, ammonium salts, carbonic acid, chlorides, free oxygen, proteins and hæmoglobin.

The bicarbonates play an important part in dealing with acid substances, carbon dioxide is eliminated through the lungs and thus the free base again combines with acids. Kidneys excrete a urine more acid than the blood. The base thus returns to the body to form bicarbonates. They are used for bringing more acid to the kidneys.

Ammonia is also formed. It combines with acid radicles which are later excreted as neutral salts.

In the metabolic process alkali reserve is being depleted. It is put back by food. If intake and production of acid and eliminations of base exceed the arrangement of regulation, acidosis takes place.

In acidosis, there is diminution of the supply of bases in the tissues and blood. There is not much change in the reaction of blood. The normal range of hydrogen ion concentration is pH 7·34 to 7·45. A good deal of addition of acid or alkali will rarely change the character of blood due to buffer arrangements of its constituents. In severe cases the capacity of blood to carry carbon dioxide to the lungs for elimination is diminished. Increased metabolic processes, as in fevers, lead to too much incomplete breakdown of protein and fat which liberates acids. Fluid loss in vomiting, purging and due to fever tend to form alkali deficit.

Weak acids, like carbonic and phosphoric, possess the remarkable property of maintaining the reaction tolerably constant. If carbonic acid is present in a solution of bicarbonates so that there are equivalent quantities of free H_2CO_3 and bicarbonate, the H-ion concentration will be exactly the same as the dissociation

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available. The present piece of work is too small to give a definite idea of the normal agglutinins but it certainly gives a rough working basis for the clinician who wants to interpret a Widal test.

Summary and Conclusion

1. 300 sera received for Wassermann reaction were examined for normal level of agglutinins.
2. 15 per cent sera showed agglutination for one or the other type of typhoid organisms.
3. O and H agglutinins may also be present and hence the corresponding antigens must always be included in a Widal test.
4. Double infections are sometimes encountered.
5. Vi agglutinins are rare.

constant of carbonic acid. Acid phosphate acts like carbonic acid in maintaining neutrality. The blood plasma contains much less phosphates than bicarbonates; the tissues contain a considerable amount which enable them to maintain their neutrality. This action of bicarbonates and phosphates is styled the buffer action.

The source of supply is partly exogenous and partly endogenous. The former source is the basic and acid substances present in the food. The endogenous source depends on the constant production in the metabolism of acids, such as, carbonic, phosphoric, lactic and sulphuric and of alkalies such as ammonia and fixed alkali. These are removed by three ways: (1) gaseous carbonic acid through lungs, (2) fixed acid through the kidneys, and (3) some of the phosphoric acid through the intestines.

When acids are added to the blood, they will be nutralised by the buffers of the plasma *i.e.*, $NaHCO_3$ (and protein). Buffer substances present in the corpuscles may also be used. The HCl from the plasma enters the corpuscles releasing base from them to combine with the added acid (*e.g.*, H_2CO_3). The HCl from the plasma entering the corpuscle combines with alkali which it receives from hæmoglobin and also from phosphates. It shows how the hæmoglobin and phosphates of the corpuscle are rendered available for neutralising acids added to the plasma. The transference of acids must go on with the other cells of the body so that the plasma has all buffer substances of the body at its disposal. The plasma is the first line of defence and the corpuscles form the second line of defence against excess of acids. A final reserve is afforded by the alkalies and some of the proteins of the tissue cells. Now, to eliminate the acid, various methods have been employed. Soda bicarb is largely used but the use of phosphoric acid is a great help. I have struck on this idea. The reserve alkalinity of blood can be measured, if wished. The ratio between the acid salts of phosphoric acid and the alkaline salts of it in blood is 1:5. In the urine this ratio varies according to the amounts of H-ion that must be eliminated from the blood. A definite amount of phosphoric acid is enabled to carry various amounts of H-ion out of the body by causing the amount of alkali excreted in combination with it to become altered. In the form of acid phosphates a given amount of PO_4 obviously carries out more H-ion than when it is excreted as alkaline phosphates. The adjustment between these two salts is a function of the kidney.

Treatment

The treatment has been based on the idea of acidosis being the important cause of hæmolysis. The kidney is helped to deal with the effete matter and neutralise and eliminate the harmful acid. Acid boric and acid sodium phosphate in doses of 15 grains each are used thrice daily. Boric acid increases the elimination of water and urea. The flushing prevents the tubules being blocked. Acid sodium phosphate unites with the acid of the lysin and helps in rapid elimination of it. The hæmolysis is thus prevented. Urine rapidly clears up. Acid sodium phosphate is internally antacid. It is a constituent of normal human blood and therein it can combine with or give off carbonic acid becoming converted into alkaline sodium phosphate and *vice versa*. It is natural acid of the urine. It is also a hepatic stimulant. The detoxicating function of the liver is thus helped.

Case Reports

Case 1—Mrs. J. D. was suffering from malarial fever, then began to pass bloody urine, inspite of big doses of alkalies. Acid boric and acid sodium phosphate cleared the urine. Quinine cured the fever.

Case 2—B. D., a pretuberculous case. Suddenly he began to pass bloody urine. He had no fever. The boric acid and acid sodium phosphate cured the condition Sometime later he developed open pulmonary tuberculosis and died of it.

Case 3—Md. I. was an old malaria case. But during a period of afebrile condition he started passing bloody urine and was cured with the above treatment.

Case 4—B. B., in the course of an attack of typhoid fever started to pass bloody urine. The above treatment cleared up the condition. About 3 weeks later he died of sudden heart failure during convalescence from typhoid fever.

Case 5—Mrs. P. G., 1-para; carrying 4 months, had bacilluria; started bloody urine. The above treatment cleared up the condition and hexamine cured B. coli infection.

Case 6—C. L. suffering from acute nephritis, had in the course of the disease hæmoglobinuria. Boric acid and acid sodium phosphate cleared the urine of blood.

N.B. Microscopically, none of the cases showed evidence of hæmaturia.

No clear case of blackwater fever was treated by this method.

Conclusion

Factors responsible for hæmoglobinuria are discussed and a line of treatment is suggested. Six cases of hæmoglobinuria successfully treated with boric acid and acid sodium phosphate are reported. The cases are far too few but the results are highly satisfactory and suggest further trial of the method.

Presence of acidosis in the cases treated by the author has not been proved.—Ed., *J. I. M. A.*

JOURNAL OF THE

INDIAN MEDICAL ASSOCIATION

CALCUTTA, DECEMBER, 1942

AETIOLOGY OF PHLYCTENULAR OPHTHALMIA

The ætiology of phlyctenular ophthalmia is still an unsolved problem though the disease with its characteristic nodular lesion was recognized in the time of Susruta[1]. An attempt to classify ocular disease on ætiological basis by Beer[2] in 1813 led him to suggest scrofulous diathesis as the cause of this disease which he grouped under scrofulous ophthalmia. Since then a vague conception of constitutional origin of the disease remained probably of its exclusive appearance in weakly children living in unhygienic conditions and fed on insufficient diet.

In course of last half a century, evidence has been accumulating to suggest that tubercular infection plays an important part although its frank tubercular nature has never been proved. The work done during recent years, inspite of the failure to demonstrate tubercle bacilli in phlyctens, have clarified to a great extent apparently confusing results and conflicting views of different observers. In his Hunterian Lecture delivered at the Royal College of Surgeons on January 30th, 1942, Arnold Sorsby[3] analysed critically and exhaustively the literature on the subject and discussed his personal experimental investigations done in White Oak Hospital and came to the following conclusions:

"Phlyctenular ophthalmia is a manifestation, not of tubercular disease, but of tubercular infection, the phlycten making its appearance only when a hyper-allergic phase is present and there is a suitable (? specific) exciting factor of endogenous or exogenous origin."

"It is suggested that the age distribution, sex incidence and seasonal variation seen in phlyctenulosis are best explained on the assumption that the affection is tubercular in character."

"The prognostic significance of the phlycten is graver than that of a positive tuberculin reaction in a child; this is borne out by the subsequent incidence of tuberculosis and mortality from it in children previously affected with phlyctenulosis."

The first part of his address which is a critical review of the literature, reveals that the phlycten is not a specific lesion but the main bulk of phlyctenular ophthalmia constitutes a clear-cut clinical entity. The disease has become much less frequent during the past forty years excepting the period of 1914-18 and its aftermath when there was a sharp rise in its incidence on the continent. It is more common in spring season, the children are mainly affected, though frequently seen in young adults, and the ratio of girls to boys is about 6:4.

Sorsby's analysis of previous works points to tuberculous infection as the underlying cause of phlyctenular ophthalmia, and the evidence for it comes from (1) a high incidence of positive tubercular reactions; (2) a high incidence of radiologically demonstrable tuberculous chest lesions; (3) finding of tubercle bacilli in the tonsils of phlyctenular patients; (4) a considerable incidence of a family history of tuberculosis; (5) a considerable incidence of a personal history of tuberculosis disease; (6) an unfavourable after-history in many cases; (7) the clinical similarity of phlyctenular ophthalmia to the sequence of the ophthalmo reaction of Calmette in tuberculous patients; (8) a significant incidence of previous phlyctenulosis in adults suffering from tuberculosis. Previous experimental studies implicate a sensitised soil as well as an exciting factor in the development of the phlycten. Sensitisation can be induced by a variety of agents, tuberculous infection being one. The exciting factor is best, but not necessarily the specific sensitising agent.

The second part of the address deals with his personal work which consists of the data on cases of

1. Krishnamurty and Bidyadhar (1941)—A Short Practice of Ophthalmology (Ancient & Modern), Published by the Ophthalmological Books Publishing Co., Chodavaram, Vizagapatam Dt., India.
2. Beer (1813)—Lehre der Angenheilkunde, Vienna, Vol. I, p. 588, taken from Sorsby's reference.
3. Sorsby, A. (1942)—*Brit. J. Ophth.*, 26:159 & 189

phlyctenular ophthalmia treated at White Oak Hospital during 1921 to 1940 and detailed investigations are recorded on the cases treated between June, 1935 and December, 1940. Each point investigated was checked in control material obtained largely from the children treated for blepharitis at that hospital.

His results confirmed the heaviest incidence in girls but does not show that malnutrition, focal sepsis and pediculosis are more frequent in phlyctenulosis than in blepharitis. It reveals a positive tuberculin reaction in 84·8 per cent of all phlyctenular cases and 81·7 per cent in cases under six. The corresponding incidence in blepharitis cases are 15·3 per cent and 8·00 per cent. The radiological evidence of tuberculosis was seen in 72·2 per cent of phlyctenular cases against 8·4 to 16·1 per cent for controls. He has found clinical tuberculosis in 6·4 per cent of phlyctenular cases against nil in control series. A family history of tuberculosis is observed in 28·9 per cent of phlyctenular cases against a computed incidence of 3·7 per cent for the normal school child population.

The sedimentation rate is raised in 79·8 per cent of cases with active phlyctenular ophthalmia. Quiescent phlyctenular cases and blepharitis show normal rates.

In none of the stomach washings of 50 cases and in the excised tonsils of 20 others of phlyctenular ophthalmia, tubercle bacilli are seen.

Lastly, the after-history of treated cases between 1921 and 1931 reveals an incidence of 5·3 per cent of clinical tuberculosis and a mortality rate of 0·8 per cent in the phlycten group against 0·8 per cent and 0·1 per cent respectively for the controls.

Thus it will be seen that the investigations carried out by Sorsby not only confirms the previous work of association of tuberculous infection as the underlying cause in the majority of phlyctenular ophthalmia but brings out the grave prognostic significance of phlyctenular reaction as compared to tubercular reaction in a child.

There is one point of special interest to the readers of this journal discussed by Sorsby and that is the problem of the "pseudo phlycten" of tropical countries. The published reports indicate a large incidence of the disease amongst adults and some histological evidence have been brought forward that the tropical phlycten tends to have an epithelioid structure.

There are hardly enough observations to accept the view that phlyctenulosis in tropical countries materially differs from those seen in Europe and the United States.

FIFTH BENGAL PROVINCIAL MEDICAL CONFERENCE

Dates—26th, 27th and 28th December, 1942.

Venue—Calcutta (B. & A. Ry. Mansion Institute, 303-1, Upper Circular Road).

President-elect—Dr. Panchanan Chatterjee, M.B., F.R.C.S.

Chairman, Reception Committee—Dr. Aghorenath Ghosh, M.B.

General Secretary—Dr. Anil Kumar Sen, M.B.

Office—164, Maniktala Main Road, Calcutta.

CASE NOTE

A RARE TYPE OF OVARIAN TUMOUR

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A local woman of Ho tribe, Jonga Kui, aged 32 years was admitted to the Hospital on 2-3-42, for pain in the abdomen and swelling in the right leg.

History—Since about a month she was noticing a lump in her abdomen, gradually increasing in size. She used to have occasional fever. For last fortnight she was having acute pain in the abdomen and she also noticed that her right foot and leg were swollen. There was no menstrual disturbance. She was married 18 years ago and had no children.

Physical Examination—The patient was in a very low condition. The spleen was hugely enlarged. Two distinct lumps were felt on two sides of the lower abdomen; the one on the right was much bigger. The lumps were hard, irregular, freely movable and tender on pressure, but not moving with respiration. The two lumps were separated by a definite gap of about 4 inches. There was evidence of slight amount of free fluid in the peritoneal cavity.

She was having remittent temperature with step-ladder like rise of the maximum, which was 99°, 100°, 102·5°, 103° and 104·5°F. on the 1st, 2nd, 3rd, 4th and 5th day respectively.

Vaginal and bimanual examinations—The uterus was small in size with a very small os. It was normal otherwise. Irregular hard lumps could be felt at both the lateral fornices. The Fallopian tubes were palpable and tender. Movements of the lump were communicated to the uterus. There was no discharge.

Investigations—Total erythrocytes—2,080,000 per c.mm., total leucocytes—5,470 per c.mm.; differential count of the leucocytes:—polymorphs—65%, lymphocytes—22%, large mono.—9%, and eosinophils —4%. No parasites were found in the blood films. Spackman-Napier's blood aldehyde test—negative; Chopra's antimony test—negative; stool and urine examination showed nothing abnormal.

Diagnosis—Diagnosis of bilateral tumour was made and its malignancy was thought of from the following features: rapid growth and hard and irregular feel of the lump, pain, presence of ascitis, œdema in the legs and low condition of the patient.

Condition of the patient was too low to undergo any surgical operation. She died on 8-3-42.

Postmortem report—Postmortem was done on 9-3-42 and the following were noted:

(1) About a pint of thick yellow fluid was found in the peritoneal cavity. (2) The spleen was very big and macroscopically was like a typical malaria spleen. (3) Both the ovaries were converted into hard, irregular, lobulated tumours with softening at places. On section the tumour was partly solid and partly cystic, with normal ovarian tissue and hæmorrhagic areas here and there. (4) The tumour of the right side was much bigger than that on the left. (5) It extended over about half of the Fallopian tubes, whole of which were markedly thickened. (6) The uterus was perfectly normal except that it was smaller in size. (7) No adhesions anywhere, no enlargement of any gland nor metastasis in any other form were found.

The whole of the uterus, ovaries and the tubes were sent to the Pathological Department of the Patna Medical College Hospital for favour of keeping the specimen in the museum and for histological examination, the report of which came as *"granulosa cell tumour."*

COMMENTS

(1) Granulosa cell tumour which has its origin in the membrana granulosa cells of the Graafian follicle is very very rare. It was first described by von Kahlden in 1895, and since then about 100 cases have been recorded by various observers.

(2) Virulence of the malignant ones is not very high, the low condition of this case seems to be due to chronic malaria she was suffering from.

(3) It is said that granulosa cell tumours of the ovary are usually unilateral, but in this case it was bilateral.

(4) The usual history of a long period of amenorrhœa followed by irregular uterine hæmorrhage was absent in this particular case.

(5) Never had such a case come to this hospital before, nor have I seen a case of granulosa cell tumour of the ovary during my last 7 years' stay in the Patna Medical College and Hospital.

ACKNOWLEDGMENT

I am grateful to Capt. A. N. Banerji, Civil-Surgeon of Singhbhum for kindly allowing me to publish this case, and to the Department of Pathology, Patna Medical College, for doing the histological examination of the specmen. I am also thankful to Rai Bahadur Dr. K. P. Mitra, former Civil Surgeon of Singhbhum, Drs. Mrs. N. S. Das, D. N. Biswas and B. K. Sen Gupta, for helping me in the study of this rare and interesting case.

CURRENT MEDICAL LITERATURE

MEDICINE

Clinical Classification and Diagnosis of Haemorrhagic Diatheses

Moloney (*New Eng. J. Med.*, 1941:225:933) writes that hæmorrhagic diseases are classified into two groups—either failure of the vascular integrity or a defective blood coagulating mechanism.

Vascular disorders are divided into nonthrombocytopenic and thrombocytopenic purpuras. The former may be due to trauma, lack of vitamins C and P, and various toxic, allergic and metabolic processes. A diagnosis of these cases rests mainly on the history and the negative laboratory data with the exception of positive capillary fragility tests.

In hæmorrhagic cases where the platelets are decreased two types, secondary and idiopathic, occur. In the secondary type, the platelet reduction is due to destruction of the marrow—this is seen in leukæmia and plastic anæmia as well as neoplastic metastasis to the bone marrow and pernicious anæmia. In idiopathic thrombocytopenia, the purpura is related to the lack of platelets—this deficiency is probably due to some mechanism of the spleen which either inhibits or destroys the platelets.

Differentiation of the idiopathic from secondary thrombocytopenic purpura is important. On the one hand an ill-advised splenectomy results in disaster, whereas in the other a successful cure is often accomplished. Bone marrow studies should be made before splenectomy is performed.

It is fairly well established that hæmophilia is caused by lack of thromboplastin.

Clinical Investigations of Curare in Organic Neurologic Disorders

Bennet (*Am. J. Med. Sci.*, 1941:202:102, Ref. *J. Bone & Jt. Surg.*, 1942:24:481) briefly describes the physiological action of curare, and then cites personal experiences with the clinical application of the drug.

He treated twelve cases of cerebral spastic paralysis with injection of ten milligrams of curare per twenty pounds of body weight every other day for a period of three to eight months. Orthopædic procedures and physiotherapy were carried out at the same time. He concludes that curare produces a definite, but transient relaxing effect upon spasticity without fixed deformity. It reduces incoordination, athetosis, and dysarthria. Favourable progress occurred in the majority of patients while under curare therapy. The treatment is not dangerous and there are no toxic reactions. Five cases of spastic paraplegia in adults, caused by transverse myelitis and advanced multiple sclerosis, were treated with curare with temporary relaxation of the spastic contractures. The effect is transient, but relief from painful spasm is afforded. The time interval during which relief is experienced is not mentioned. One case of status epilepticus, secondary to a toxic encephalitis, which had failed to respond to various sedative and other anæsthetics over a ten-day period, was treated with curare. The child had had seizures every few minutes. When seen, the child was moribund; but during twelve hours of treatment before death he was completely relaxed.

Six patients with encephalitic parkinsonism, oculogyric crises, and paralysis agitans were relieved of their tremor and rigidity for one hour, but were unable to carry out active movements.

Four patients with Huntington's chorea were relieved of their incoordinate movements for a few hours. The author states that this is the only drug that had any effect on the involuntary movements in the disease.

Temporary relaxation lasting one hour occurred in a number of cases of athetosis and dystonia. Temporary results were likewise seen in two cases of tetanus.

The author concludes by stating that although the action of curare is transient, continued experimentation should produce a sustained action. He briefly mentions a synthetic drug, quinine methochloride, which has a curare-like action, effective orally. Curare acts at the motor end plate and inhibits the action of acetyl choline on voluntary muscles.

Standardization of the Treatment of Arthritics

Pemberton (*Practitioner*, 1942:148:164) deals with the subject under the following heads:

Rest—The first recommendation which should be made in the direction of care of any given group of arthritics should be rest, not only local but systemic. It would be better, however, if recommendations could be made for each of those things which rest brings about rather than to order to rest as a blanket prescription.

Diet—The presence of the following pathological conditions must be taken into consideration in the choice of diet, *viz.*, a tendency to tissue œdema, avitaminosis, atonic condition of the gastrointestinal tract with hypo or achlorhydria.

Physical therapy—It also plays an important adjuvant role. However, even in well reputed spas, emphasis upon this measure may be unduly great and many instances are seen in which the principles of rest has been violated, Osa has been piled on Pelion, and faulty and painful joints have been injured by what was, in fact, further trauma.

Drugs—Mild sedation in the form of sodium bromide or phenobarbitone may be necessary as also stimulation with nux vomica (tincture nux vomica in 3 minim doses, thrice daily). Endocrine therapy has definite application to selected cases.

In order to bring to focus, however inadequately, the general point of view outlined above, there is herewith appended a sequence of steps which, in the opinion of the author and his associates, should underlie any large-scale attempt at the treatment of arthritics as a group. (1) Rest, systematic as well as local. (2) Sedation and/or stimulation. (3) Optimal nutrition in the refined sense already discussed. (4) Proper

gastrointestinal function. (5) Examination of blood chemistry. (6) Time for establishment of a general equilibrium. (7) Examination for foci of infection. (8) Medication, such as iron, arsenic and nux vomica. (9) Treatment of foci conservatively. (10) Use of physical therapy conservatively—meaning chiefly heat, gentle massage, postural exercise. (11) Orthopædic help. (12) Endocrine therapy in selected cases. (13) Psychological reeducation. (14) Lastly, if at all, vaccines or gold.

Assay of Liver Extract on Bone Marrow

Pace and Fisher (*J. Pharmacol. & Exp. Therap.*, 1942: 74, Ref. *M. Press.*, 1942:208:99) write that there has been a lack of a rapid and easily available and satisfactory method for the determination of the potency of liver concentrates. They report on a method previouly devised by Overbeck *et al* in which marrow preparations are used. Briefly the technique is as follows: Pieces of marrow from the young guineapigs were placed in dishes of plasma from the same pig and varying dilutions of liver extract added. After incubation at 37°C for 15 hours, a zone of migration of cells from the marrow into the surrounding plasma could be made out. A chart is constructed from the varying dilutions and it is found that this chart corresponds closely with the clinical potency of the extract tested. Destruction of P. A. by boiling with sulphuric acid prevents the expected peak on the graph and extracts which are not active clinically also show no peak. The method seems to indicate a method of assay for 'P.A.' factor potency.

Treatment of Pre- and Post-operative Gastric Retention: Gastric Tetany as a Symptom

Gambill and Shape (*Proc. Staff Meet. Mayo Clinic*, 1942:17:72) write that tetany is merely a symptom and treatment of tetany itself seems relatively unimportant. The underlying physiological disturbances must be recognised and corrected and early and frequent studies of blood chlorides, carbon-dioxide combining power of the blood and blood urea are essential for determining these disturbances in any case of persistent emesis. Gastric tetany, whatever may be the exact mechanism concerned, is usually associated with (*a*) alkalosis, (*b*) hypochloræmia, (*c*) a normal value for serum calcium and (*d*) dehydration. Thus, treatment consists of combating alkalosis, hypochloræmia, and dehydration by (*a*) giving adequate amounts of glucose and solution of sodium chloride, (*b*) by avoiding unnecessary gastric aspiration, (*c*) by avoiding absorbable alkali in states of alkalosis or in obstructive gastric lesions with emesis or in renal insufficiency and (*d*) by surgical correction of the obstructing lesion.

Treatment of Asthmatic Paroxysm with Nicotinic Acid

Maisel and Somkin (*J. Allergy*, 1942:13:397) from the analysis of the results obtained in 21 patients who received intravenous injections of nicotinic acid (0·1 gm.) for relief of asthmatic paroxysms observe that 16 or 76 per cent were definitely improved from varying periods of 3 to 15 hours, that of the 9 patients receiving only oral therapy, 5 were likewise benefited and that of 18 patients who received intravenous therapy followed by oral therapy, 11 showed decided improvement in their asthma. Nicotinic acid orally (in doses of 0·2 gm. before meals and on retiring) was, therefore, efficacious in about 60 per cent of the patients both for the control of acute attacks and for the continuous wheezing. The clinical manifestations following the administration of nicotinic acid are characterized by a flush and sensation of heat. The flush occurs 3 to 5 minutes after an intravenous injection and is confined mainly to the face, neck, chest and upper arms. The sensation of heat precedes the flush and is of shorter duration. The patients who were relieved with nicotinic acid following the appearance of the flush breathe more freely—they often begin to cough and expel tenacious mucus. It is not known at present if nicotinic acid exerts its therapeutic effects by relieving bronchospasm or whether it in some way directly affects the pulmonary vessels. Nicotinic acid is not offered as a substitute for ephedrine or epinephrine but it may act as an adjuvant or it may serve as a substitute when ephedrine is ineffective or when the patient becomes epinephrine fast.

The Effects of Diphtheria Toxoid on Painful Enlarged Nerves in Leprosy

Collier (*Internat. J. Leprosy*, 1941:9:177, Ref. *Trop. Dis. Bull.*, 1942:39:231) records 4 cases in which the administration of diphtheria toxoid was followed by relief of the pains in cases of enlarged nerves of leprosy. Previously operation on such painful nerves had only given temporary relief on account of the formation of scar tissue. It is stated that the new treatment has given satisfactory results in more than 300 cases. Temporary hot and itching sensations and increased pain in the hands and feet may occur after the injections.

Diphtheria Toxoid in the Treatment of Leprosy: Clinical and Immunological Investigations

Davison and Grasset (*Leprosy Rev.*, 1941:12:68) report on the use of diphtheria formol toxoid in leprosy in South Africa in doses of 0·5 c.c. increased to 10 c.c. over a period of seven months according to the suggestions made by Collier and the results were assessed nine months from the beginning. In 16 patients the Schick test was carried out before immunization and their blood antitoxin titrated before and after treatment with satisfactory immunization response in a mojority. There was no corelation between the antitoxin titre after the toxoid treatment and the clinical changes in the treated patients. The treatment was voluntary and only 71 out of 100 were willing to complete the full course, although leprosy cases will persevere with any treatment when they can observe any improvement. Out of these cases who completed the course 12 became worse, 34 showed no appreciable clinical change, 21 showed slight improvement and 5 only a marked improvement or 6·94 per cent compared with 50 per cent or more claimed by Collier in Thailand. The authors also could not agree with Collier's theory that suprarenal inefficiency was a necessary predisposing cause of leprosy; they in their experience of 5000 cases could not see a single case of such gross deficiency; in 100 unselected cases the blood pressure record was entirely within normal limit and there was no anatomical degeneration of the suprarenals in eight successive postmortems of non-treated cases. The authors also could not give any satisfactory explanation for the limited results as compared with those by Collier.

SURGERY

A Plea for the Earlier Diagnosis of Rectal Cancer

Brand (*New York State J. Med*, 1942:42:33) writes that much progress has been made in the treatment of carcinoma of the rectum though many cases are still not diagnosed early enough. The symptoms described in text books are those of the late stage. Any symptom, however mild, that focuses the patient's attention to the rectum may be due to cancer. Analysis of the author's 108 cases reveals the following points: 31 or 28 per cent gave a history of cancer in relatives, 10 of whom had cancer of the rectum; blood in the stool was complained in 87 patients, in 32 of these as the first symptom; constipation in 51, in 30 as the initial symptom; flatus in 47, in 28 as the first symptom; diarrhœa in 36, as the first symptom in 12; pain in 36 and as the initial symptom in 4; mucus in 31, in one patient being the first symptom; loss of appetite in 1 patient as the first symptom; loss of weight in 20 cases, change in size of the stool in 18, tenesmus in 14, obstruction in 8. The average interval from the onset of symptoms to the time of seeking advice was 8-9/10 months. Of the 108 patients 8 came to the clinic directly, in 25 an early diagnosis was made and in the remaining 75 there was an average delay of 10 months from the time they were first seen until they were referred to the clinic—in 50 per cent the delay was due to misdiagnosis and of the 100 patients, 20 had not even received a rectal examination. The author makes a plea for careful attention to all bowel symptoms, no matter how mild, and a thorough examination.

Progress in Bone and Joint Tuberculosis

Harris and Coulthard (*J. Bone & Jt. Surg.*, 1942:24:382) from an analysis of the results of treatment and from a consideration of the factors which influence the end results in 307 cases treated in the bone and joint wards of the Weston Sanatorium during the years 1931 to 1940 point out the following salient facts:

1. Bovine tuberculosis is no longer a factor of any significance in the causation of bone and joint tuberculosis among adults in Ontario.

2. Adequate treatment of bone and joint tuberculosis demands adequate provision for rest as well as adequate provision for surgery.

3. Prognosis is affected favourably by two factors in particular: (*a*) Adequate treatment of abscesses, so as to prevent secondary infection of bone,—the existence of an uncontaminated tuberculous abscess need not affect the prognosis adversely. (*b*) Freedom from multiple lesions of tuberculosis in the body.

4. Secondary infection of various joints has the following effects: (*a*) of the spine renders the prognosis almost hopeless; (*b*) of the sacro-iliac joint and hip renders the prognosis poor; (*c*) of the knee, ankle, or foot requires excision or amputation; (*d*) of the joints of the upper extremity greatly prolongs hospitalization,

5. Multiple lesions of tuberculosis are to be found in a high proportion of cases as follows: (*a*) Pulmonary tuberculosis in over 40 per cent. (*b*) Multiple bone tuberculosis in almost 30 per cent. (*c*) Genito-urinary tuberculosis in over 20 per cent.

The prognosis is affected adversely by the presence of these complications, their importance being in the order named.

6. More than one-third of all patients were free from multiple tuberculous foci. The percentage of arrested disease and the ability to return to work in these patients was high, especially in the cases of tuberculosis of the spine (80 per cent) and of the knee (100 per cent.). The mortality rate was 13 per cent and was usually due to secondary infection of bone, or to non-tuberculous disease.

7. Almost one-quarter of all patients had additional tuberculosis in other bones, or in the genito-urinary system, or in both, but not in the lungs. In these, the treatment has to be long enough to arrest tuberculosis throughout the body, and more than one operation is usually required. The incidence of return to work is much reduced and the mortality rate rises to about 20 per cent, due to the appearance of meningitis and of Addison's disease in addition to chronic suppuration and non-tuberculous disease.

8. Over 40 per cent, of all patients had pulmonary tuberculosis, the most serious of tuberculous complications. When this is combined with other skeletal and renal foci the prognosis is very much worse then when pulmonary tuberculosis is the only complication, the incidence of arrested disease and of return to work in the latter being between 40 and 50 per cent, and in the former between 12 and 20 per cent. The mortality rate rises from 38 per cent in the latter to between 44 and 80 per cent in the former, the outstanding causes being miliary tuberculosis, meningitis, and pulmonary tuberculosis.

9. Tuberculosis of the spine was arrested in 88 per cent of patients treated by spine bone graft, but in 26 per cent the arrest of the systemic disease was delayed or entirely prevented by tuberculosis elsewhere in the body.

10. The best results are to be obtained by treating bone and joint tuberculosis first by rest and by controlling other tuberculous foci in the body; then by operation to secure bony ankylosis of the affected joint because the results following this are superior to those obtained by the fibrous ankylosis or unstable joints which so often mark the end result of non-surgical treatment.

Co-ordination of Physical Methods in the Treatment of Peripheral Nerve Injuries

Cooksey (*Brit. J. Phys. Med.*, 1942:5:23) points out that the reactionary œdema in a limb after trauma is the first and most potent cause of muscle atrophy and joint stiffness and when the vasomotor, sensory and motor nerves are divided the harmful effects of œdema are increased greatly. It is of primary importance, therefore, that reactionary œdema should be prevented as far as possible or effectively controlled as soon as established. This is done by posture, supports such as plaster of Paris or elastic webbing bandages and massage. Postural drainage by elevation of the injured limb is the most effective; certain elastic bandages are also quite effective especially when applied after massage twice a day. Massage is good in reducing œdema but it is of no use unless the limb is elevated or supported by elastic bandages between treatments. In a case associated with a fracture the use of plaster of Paris is essential but then the limb should

be elevated in the splint and the joints not included in the plaster should be moved—all that is necessary is the early co-ordination of treatment. The final result of nerve injuries often depends on the excellence or otherwise of the surgical care applied soon after the injury and co-ordination of the physical methods starting at that time.

Sulphonamide Therapy of Trachoma

Smith and others (*Am. J. Ophth.*, 1941:24:174) give in the following lines the summary and conclusions of their study:

1. Following the use of sulphanilamide *per os* in 26 patients the disease in 2 was arrested, 11 were improved and 13 unchanged at the end of the treatment. 2. Following neoprontosil applied topically a definite improvement was observed in all of 9 patients; all were subsequently given some other form of treatment in order to render them asymptomatic. 3. A review of the correlated literature has been made and the results have been analysed. 4. A conservative opinion at the present time would be that sulphonamide compounds cause a disappearance of the nonspecific (that is, subjective) symptoms of trachoma and an improvement of varying degrees in the clinical condition; evidence of their curative capacity remains to be established. 5. It is the opinion of the writers that in spite of the improvement, recovery from trachoma is not the rule but the exception. 6. It, therefore, seems the wiser procedure to supplement sulphonamide treatment with one of the more usual forms of local therapy.

A Case of Sympathetic Ophthalmia Treated with Sulphanilamide

Gamble (*Am. J. Ophth.*, 1941:24:49) reports the case of a boy with a perforating injury of the right eye in whom sympathetic ophthalmia developed. This had apparently improved with the use of sulphanilamide when the boy died from an accident. Pathologic examination of the both eyes proved the diagnosis of sympathetic ophthalmia.

Vitamin D in Vernal Catarrh

Knapp (*J. Allergy*, 1942:13:407) writes that vernal catarrh is believed to be an allergic condition and has been found associated with axial myopia and keratoconus and in this condition the administration of vitamin D (Viosterol) and calcium (in the form of mineral mixture tablet) has proved to be of real value. In a series of 47 consecutive cases of vernal catarrh, 42 received the therapy. 60 drops of Viosterol (13,860 units) were given after the meal. The mineral mixture tablet contained the following in milligrams: calcium 140, phosphorus 83, iron 1, copper 0·05, magnesium 2·8, sodium 5 and potassium 5. It is given before meals in doses of one tablet if the patient drank 1 quart of milk and for each glass less than a quart 2 tablets more. The patients of the series represented the various types of vernal cararrh and 42 out of 43 showed definite improvement, and the improvement in 25 cases proved to be superior to that effected through several other accepted therapeutic measures. These results go to show that there is a disturbance of the vitamin D-calcium-phosphorus metabolism in vernal catarrh.

OBSTETRICS AND GYNAECOLOGY

Effect of Progesterone on Uterine Contraction

Bickers (*Am. J. Obst., & Gynec.*, 1942:43:663) writes that uterine contractions before and after the administration of synthetic progesterone subcutaneously have been studied by means of an intrauterine baloon connected to a mechanical ink recorder which recorded the contractions on a kymograph. The drug has no effect on uterine contractions in the normal ovulatory cycle, either during the follicular or the corpus luteum phase; it has no effect on the high amplitude, hypertonic contractions of primary dysmenorrhœa nor on the uterine contractions in threatened abortion or in the puerperium.

The Effect of Pregnancy and the Puerperal State on the Growth of Malignant Tumours

Mankin (*Arch. f klin. Chir.*, 1940:199:337, Ref. *Am. J. Obst. & Gynec.*, 1942:43:1075) from a careful analysis of clinical developments in a considerable series of cases in which a pregnancy was complicated with a malignant growth somewhere in the body observes that the pregnancy by itself does not accelerate the growth of the malignant tumour, but the deleterious effect follows labour, abortion, puerperium and lactation. This holds true for cancers in the breast, uterus, intestinal tract, etc. Therefore nothing is gained by interruption of the intercurrent pregnancy and as a matter of fact, continuation of gestation to term often affords valuable time to deal with the malignancy before the puerperal or postabortal stage begins its inevitable aggravating effect.

A Comparative Study of Tubal Insufflation and Lipiodol Injections in Sterility

Feiner (*Am. J. Obst., & Gynec.*, 1942:43:639) from the studies based on the result of the investigation of tubal patency in 706 consecutive cases observes that carbon dioxide insufflation should always precede the use of lipiodol as it gives all the necessary information in the majority of cases without some of the drawbacks of lipiodol and the use of lipiodol should be reserved in the main for those cases of nonpatency in which accurate localization of the obstruction is desired. The therapeutic value of uterotubal insufflation is seen in many ways in cases of partial obstruction; a greater or more normal degree of patency may be established in certain cases showing a complete obstruction. Tubal patency can be re-established by the breaking down of adhesions, the expulsion of plug of mucus or strengthening out of kinks. Dysmenorrhœa is sometimes relieved; pregnancy follows insufflation in certain cases. The author holds the view that lipiodol injections are not harmless and that as a diagnostic method lipiodol injections carry a morbidity and mortality even though small. In cases of sterility in which one tube is occluded or both tubes show partial obstruction as demonstrated by air insufflation, lipiodol should be used cautiously as complete occlusion may result.

RESECTION OF THE STOMACH

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Benares

Before Billroth dared to remove a cancer of the stomach he ordered his pupils Gussenbauer and v. Winiwarter to study the gastric resection on dogs, in order to get detailed information about the chance of such an operation. Already previous to that, Billroth has shown, that there was a possibility of suturing the wall of the stomach as well as the intestinal wall. The first resection of the stomach on account of a carcinoma was made by Billroth on January 25th, 1881. At that time he had a female patient with a carcinoma in the region of the pylorus. This tumour was removed by Billroth and the stump of the stomach anastomosed end to end to each other. The result was favourable.

Already in 1879 Pean and in 1880 Rydygier performed resection of the stomach for carcinoma, but both the patients died after the operation. Pean's patient died after 5 days, and Rydygier's after 12 hours. Both the surgeons knew already about the experiments of Gussenbauer and v. Winiwarter and made the operation according to the techniue of those two surgeons.

Billroth is, therefore, the first surgeon, who introduced this operation in surgery and his name will always remain connected with this operation. The method, which Billroth used in his first operation is also called Billroth I method.

Four years after his first resection of the stomach, Billroth operated again on a patient for pyloric carcinoma on January 13th, 1885. In this case, the tumour was so large, that Billroth decided to make first of all a frontal gastro-entero anastomosis, and since the operation was done so strikingly quick, Billroth also removed the carcinoma afterwards and sutured the duodenal surface of incision as well as the surface of incision of the stomach blind, which means each one separately. Thus the method Billroth II was created. This method is used by most of the surgeons to day and that not only in cases of carcinoma, but also in ulcers. Of course, this method has been modified by many surgeons, just as the method Billroth I.

Modifications of the Method Billroth I

Original Billroth I—After resecting the pars præpylorica, the duodenum is directly anastomosed with the stomach. The duodenum is in its lower part implanted into the stomach close to the large curvature on account of the dissimilarity of the transverse incision of the duodenum and of the stomach, the remaining part of the surface incision of the stomach is sutured (blind) sac-like.

Modification according to Haberer—In order to make the sac-like (blind) closing of the surface of the incision of the stomach unnecessary, the larger transverse incision of the stump of the stomach is diminished to the size of the incision of the duodenum by means of a raking suture and now the stump of the stomach gets anastomosed end to end with the duodenal stump. Sometimes it is very difficult to anastomose the stump of the stomach with the duodenal stump, without taking a risk of a too big tension. In order to avoid that, Haberer suggested to anastomose, end to side, the descending duodenal peduncle with the transverse incision of the stomach.

Modification by Kocher—Kocher closed the stump of the stomach completely sac-like (blind) and implanted the duodenal stump end to side in the posterior wall of the stomach.

Modification of the Method Billroth II

Original Billroth II—After resecting the pars præpylorica, the duodenal stump as well as the stump of the stomach are sutured sac-like (blind) and an anterior gastro anastomosis is done.

Modification according to Kroenlein-Hacker-Mikulicz—The jejunum is implanted only in the lower part of the stomach in the form of an anterior anastomosis. The upper part of the stomach, lying close to the small curvature, is sutured sac-like (blind).

Modification according to Reichel-Polya—The upper jejunum loop is retrocolic anastomosed, end to side, with the entire surface of the stomach.

Modification according to Hofmeister-Finsterer—The upper jejunum loop is only retrocolic anastomosed, end to side, in the lower part of the surface incision of the stomach. A small part of the surface incision of the stomach is sutured sac-like to the small gastric curvature.

The Technique of the Resection of the Stomach at the Eiselsberg Clinic

At the Surgical Clinic of Vienna, there have been 2766 resections within the years 1901-1930; of these 1261 were cases of gastric ulcers, 937 of duodenal ulcers and 568 of carcinoma of the stomach.

There were in gastric ulcers 49 deaths out of 1261 cases and in duodenal ulcers 40 deaths out of 937 cases. It is mentioned that among these numbers of mortality were included also cases of delayed death and cases with perforation.

Preparation of the patient—In cases of gastric and duodenal ulcers, an evacuation of the stomach before the operation is advisable. It simplifies, especially in cases of dilated stomach, the operation very much and besides, reduces the danger of pneumonia due to food in the bronchi in those cases, which are operated under general anæsthesia. In cases of narrowing ulcers in the region of the pylorus or of the duodenum, as well as in cases of carcinoma of the stomach it is of much help, not only to evacuate but also to wash out the stomach before the operation. The dangers of the operations become reduced to a great extent, when the obstructed and decomposed content of the stomach is removed and one should never fail to make an evacuation of the stomach immediately before the operation even in cases of perforated gastric or duodenal ulcers.

Part of the cases is operated under general anæsthesia, whereby either ether anæsthesia or lately also the laughing gas anæsthesia is used. The laughing gas is either used alone or in combination with local anæsthesia when it fails to reduce the muscular relaxations, which occurs in most of the cases.

The local anæsthesia is used in all those cases, where either the patient wishes this kind of anæsthesia, or where the general condition of the patient, the old age, the conditions of the lung or of the heart, make the local anæsthesia desirable. More

than two-thirds of all gastric resections are done under local anæsthesia. For that ½ per cent novocaine adrenalin solution is used.

The local anæsthesia is begun according to Braun's suggestion with the infiltration of the abdominal wall in the middle line between the ensiform process and the umbilicus. After opening the peritoneal cavity the peritoneum is anæsthetised right and left from the laparotomy incision by means of fan-shaped subserous injections, in order to prevent the pain, caused by the-then-setting of the laparatomy blunt hooks. The stomach is much carefully displaced further below, and the fingers of the left hand palpate the upper margin of the pancreas very exactly. The left index-finger searches above the pancreas the vertebral column and the right edge of the aorta which is distinctly felt by the pulsations and pushing the aorta somewhat towards the left side. The tip of the index finger remains in lying position and the right hand of the surgeon sets now a long and fine needle into the abdominal cavity along the left index finger. The needle is placed near to the right edge of the aorta and is sufficiently at a distance from the inferior vena cava. By drawing the needle back about 2 to 3 mm. the point of the needle leaves the vertebra and lies now in the retro-peritoneal space. After waiting only for a few seconds it is seen, whether blood is drawn into the syringe or not. If so, a vessel has been punctured and the injection must be left undone. But if there is no blood 60 c.c. of a ½ per cent solution is slowly injected. Also the small curvature of the stomach, close to the cardia, is infiltrated with the novocaine solution, in order to interrupt the vagus nerve and to reduce the disagreeable feeling of the dislocation of the stomach during the operation. Besides this, the transverse colon is lifted up, the transverse mesocolon as well as the mesenteric root exposed and about 30 c.c. of the narcotic solution is infiltrated by several injections below the visceral duplicature. This as a rule finishes the local anæsthesia in most of the cases. The total quantity used of the solution is about 150 c.c. The anæsthesia is as a rule so complete, that not one drop of another general anæsthesia is necessary. In order to obtain a good local anæsethesia every individual manipulation at the abdominal organs must be done most carefully.

Methods of resection of the stomach—This dissertation shall only be limited to the description of the most used methods of to-day. Hitherto belongs primarily the method Billroth II, which is especially chosen in carcinoma of the stomach, while it is much more a radical operation. Next to that comes the method Billroth I, further the resection for exclusion, which nowadays is especially used more and more in those cases of deep duodenal ulcers, in which the radical removal of the ulcer would increase greatly the danger of the operation. In addition to that, the process of the removing of the relapsing jejunal ulcer (ulcus pepticum jejuni) shall be mentioned in the supplement.

Laparotomy and the diagnosis of the gastric disease—The abdominal cavity is opened exactly in the median line, along the linea alba. The incision begins below the ensiform process and reaches down to the umbilicus. In those cases, where the patients have a thin abdominal wall, or they have a broad angle of the lower thoracic aperture, the laparotomy incision is not made right down to the umbilicus, but it ends to a point of two fingers above the umbilicus. This preserves the right tension of the umbilical fascia whose importance Schmieden mentioned at the Surgical Congress, 1928 and diminishes very essentially the possibility of the occurrence of post-operative hernia. Besides all that, it also simplifies very much the closing of the laparotomy wound.

The first attention after opening the abdominal cavity must be given to the nature and the origin of the disease in the stomach. For this reason the laparotomy wound is held open for a short time by means of simple spatulas (as used for the abdominal wall), from the two assisting surgeons. In cases of carcinoma not only the size of the primary tumour but also the extension of the metastases are taken into consideration. It often happens that the suspected ulcer which has been diagnosed by the x-ray examination is not found after the peritoneal cavity is opened even if the gastric wall has been most carefully palpated for the presence of any thickening. In such a case it would be a great mistake to close the abdominal cavity and deny the presence of an ulcer. In this case it is absolutely necessary to cut a window in the gastrocolic ligament, to have a chance to look into the omental bursa. From this window one is able to see the posterior wall of the stomach, of the duodenum and also the entire pancreas. This also enables him to find even the smallest ulcer, either at the posterior wall of the stomach or close to the small curvature which could have been never seen without the window. In those cases where even by means of the window no ulcer could be found, the window in the gastrocolic ligament is closed by 2 or 3 sutures, without any disadvantages for the patient, and the laparotomy wound is also closed again. This very same window in the gastrocolic ligament also enables one to estimate the extent of the penetration of gastric ulcers into the pancreas as well as the size of the ulcers on the posterior wall of the duodenum and the possibility of their breaking through into the pancreas. At Eiselsberg Clinic, every resection of the stomach begins with the opening of the omental bursa. Before a resection of a duodenal ulcer is decided on attention is paid to the common bile duct. The region of the hepato-duodenal ligament is made visible, the position of the common bile duct is diagnosed and its resection from the aboral edge of the ulcer is most carefully examined. This holds good especially for ulcers which are placed deep in the duodenum, but it is advisable to get well acquainted with the position of the common bile duct at the beginning of the operation in every case of duodenal ulcer, as well as in cases of gastric ulcer. This safeguards disagreeable surprises which lead to difficulties when finishing the duodenal stumps and which may even cause a postopening of the stump or a stenosis of the common bile duct. The right time diagnosis of the little distance of the common bile duct from the ulcer gives a chance to refuse the radical resection of the ulcer and to choose the resection for exclusion or the gastroentero anastomosis instead. According to the experi ence obtained in the Clinic the examination of the position of the common bile duct previous to the beginning of the operation is considered very valuable and it should not be, by any means, neglected in a case of resection of the stomach.

Items for resecting the entire pars præpylorica—The purpose of resection, especially in cases of gastric or duodenal

ulcers rests, nothing to say about the resection of the ulcer, in the removal of the entire pars præpylorica.

The following procedure, as advocated at the Clinic gives a sure proof of the necessity for, the entire removal of the pars præpylorica:

The gastrocolic ligament is spread out along the large curvature of the stomach and a view is taken of the vessels. Along the large curvature at a distance of about 1-2 cm. runs a vascular arch in the gastrocolic ligament which is created by the connection of the right and left gastro-epiploic arteries. From this vascular arch, fine branches of vessels run to the large curvature in radiating direction, which are further distributed in the wall of the stomach. If the large curvature is now expanded and a view of the distribution and number of these fine vascular branches is taken it is easy to state that the number of these fine vessels within that part of the large curvature, corresponding with the caudal half of the stomach is comparatively larger than that along the part of the curvature which belongs to the cranial half of the stomach. But these running vessels placed tightly and parallel to each other become so scarce, beginning at a certain point of the large curvature, that the distance from the individual vessel is about 3 cm. This makes places in the gastrocolic ligament which are poor in vessels, just as are found in the mesocolon. This place of the large curvature of the stomach, where the vessels become scarce, does not only make the border between the fundus and the pars præpylorica, but this place can also very easily be found externally, on account of the vascular branches. Up to this place resection is done along the pyloric half of the stomach at Eiselsberg clinic. At the small curvature the left gastric artery serves as a sure guide in that line. The left gastric artery comes from the aorta, runs in the small omentum and turns archshapedly to the small curvature. That place, where this vessel comes in close neighbourhood of the gastric wall the stomach is incised by the resection corresponding to the small curvature. If this place is connected with the previously mentioned point at the large curvature, the line of demarcation is created inside of which the stomach is cut into two in the operation.

Method Billroth II

Preparation of the stomach and of the duodenum for resection—From the window, which has been made at the beginning of the operation in the gastrocolic ligament, the ligament is lifted in small sections by means of an aneurism needle right at the large curvature and every section is tied threefold, and cut into two (two ligatures remain at the ligament and one at the large curvature). This tying up and cutting of the ligament proceeds towards the fundus up to the previously mentioned place of the large curvature. Similar to that is the ligament parted from the large curvature towards the pylorus. It is of great importance to make the ligature of the ligament right at the large curvature, for it prevents grasping the middle colic artery into the ligature. Near the pylorus and the duodenum the ligament divides into two parts, the one goes to the stomach and the other to the duodenum. There the part which runs to the duodenum is ligated in several sections and the lower edge of the duodenum which lies in continuation of the large curvature is thus freed. The other part of the ligament running to the stomach becomes visible and is likewise tied up, whereupon the posterior wall of the duodenum, running from the duodenum to the head of the pancreas, is exposed. These fine bands of tissue fibres (every one of them may have vessels) may by no means be divided without being ligated producing hæmorrhages which would surely interfere with the operation.

Of great adjuvant remedy for this preparation at the posterior wall of the duodenum and ligature of the numerous bands of tissues is the fine needle matching with the aneurism needle, as introduced by E. Novak from Eiselsberg clinic some time ago. Thus the necessary length of the posterior wall of the duodenum is most carefully exposed without taking a risk to injure the pancreas. The surgeon takes the duodenum in his right hand and lifts by means of the Kocher's needle that bridge of tissue of the small omentum which lies at the upper duodenal edge near the pylorus and contains the right gastric artery. This bridge is ligated fourfold and then cut into two. Two ligatures remain at the stump of the small omentum, one ligature and one acupressure ligature remains at the small curvature of the stomach.

The acupressure ligature (it is applied towards the stomach) serves to increase the safety of stopping the hæmorrage. Even most carefully applied ligatures, which remain after the separation of the small omentum towards the stomach, are liable to slide off, for in this part of the operation, the stomach is lifted up by the assistant and thus the small curvature gets stretched. They cause then much trouble and much time is wasted in trying to stop the bleeding. In order to avoid this unfavourable event, an acupressure ligature is applied.

The small omentum sends here bands of connective tissue partly to the duodenum, partly to the pancreas. These tracts of tissue fibres must be ligated separately and cut into two. The upper edge of the duodenum is exposed to the same extent as the lower duodenal margin by further ligatures, simplified by the previously stated position of the common bile duct and the small omentum still left is ligated and cut towards the fundus. The incision of the duodenum is continued for such a length of time (without endangering the bile duct) until the duodenum can be cut through distant from the ulcer and the remaining duodenal stump can be closed without difficulties. The ulcer may not always have to be removed in toto, for a peptic ulcer has no similarity to a malignant neoplasm. In cases of deeply placed duodenal ulcers, the line of demarcation runs very frequently right through the ulcer, giving thus a chance for the remaining aboral half of the ulcer to be included in the closing suture of the duodenal stump. This procedure does not only enable one to close the stump of the duodenum very carefully but also saves some parts of the duodenal wall. Finally the right hand of the surgeon grasps the small curvature of the stomach from below at that place, where the left gastric artery joins the small curvature, puts these last remains of the small omentum, containing the left gastric artery on the Kocher's curve needle, ligates it fourfold and cuts the tissue into two. Two ligatures remain at the end of the small omentum and are grasped into a clamp with sliding catch, the third ligature and one acupressure ligature remain at the small curvature. It sometimes may happen in those cases where the small omentum is rich in fat that the wall of the stomach of the

small curvature upto the lumen of the stomach is injured when trying to put the last remains of the small omentum near to the small curvature on the Kocher's needle in order to apply the ligature and separate it, because it is very difficult to find the border between the wall of the stomach and the omentum, due to the big quantity of adipose tissue. In a case like this as a matter of precaution the serosa of the omentum is incised just a little at the probable place, the omentum is pushed from the wall of the stomach by means of an anatomical tweezer—a procedure, which can be done without any bleeding. Thus the wall of the stomach becomes distinctly visible and the injury is definitely avoided. Right at this place, the small curvature must be freed from the small omentum and from the adipose tissue, because here the serosa-sutures of the stomach jejunum anastomosis is to be applied in the latter course of the operation. Thus, that part of the stomach and of the duodenum, which is to resect, is now prepared, and right there is the moment to begin with the resection.

In those cases where the ulcer of the posterior wall of the stomach has broken in into the pancreas, the ulcer is sharply separated from it. In those cases where the duodenal ulcers have broadly broken in into the pancreas, the radical removal would not only cause a considerable loss of the posterior duodenal wall but also induce an injury of the pancreatic tissue. Here one much prefers and nearly always makes the resection for exclusion or the gastro-entero anastomosis.

Care of the duodenal stump—The resection begins with the transverse separation of the duodenum (in cases of gastric ulcers right behind the pylorus, in duodenal ulcers aboralwards from the ulcer). The assistant lifts the loosened stomach with both his hands at the small and at the large curvature, whereby also the duodenum gets drawn up. The field of operation is covered with clothes; and whether dealing with a gastric or a duodenal ulcer small intestinal crushing forceps (according to Payr) are applied to the appropriate place of the duodenum. At a certain distance from this forcep, the duodenal clamp (according to Brunner) is applied towards the pylorus. The duodenum is sutured with a straight needle by an uninterrupted quilting suture right below the Payr's forceps and then transversely separated right above the Payr's forceps; the Payr's intestinal crushing forceps is then removed. This cutting into two may be either done by knife or with the electric loop. The stump of the duodenum thus closed is lifted up by the assistant on both the ends of the uninterrupted suture, while the stomach, now separated from the duodenum, is placed over the left costal arch. Previous to that the oral end of the duodenum which has been closed up by the Brunner's clamp is wrapped in a compress. Two more rows of sutures are now added to the duodenal stump, which has been already closed by the uninterrupted quilting suture. The second row of suture begins with a half purse-string suture on both the ends of the duodenal stump. This half purse-string suture grasps the posterior wall of the duodenum further the upper margin of the duodenum and finally the anterior duodenal wall. While this suture is pulled, that end of the duodenal stump which corresponds with the small curvature side is turned up and the thread is knotted. Thus the end disappears in the depth. The very same procedure is correspondingly done to the lower edge of the duodenum, so that also the end of the duodenal stump which appropriates to the large side of the curvature disappears. Especially much attention is given to the taking care of those two places. Between those two corner sutures, several interrupted sutures are applied which grasp the anterior as well as posterior wall of the duodenum and the first uninterrupted suture in covered by pulling the thread. The third row of suture consists of Lembert-like interrupted silk sutures, whereby the posterior as well as the anterior wall of the duodenum, are grasped into the suture, the anterior wall to a much larger extent, so that the serosa-freed posterior wall is covered from the serosa of the anterior wall. When grasping the posterior wall of the duodenum, great attention must be given that at the most the capsule of the pancreas is taken into the suture, but not the glandular tissue itself. This way of closing the duodenal stump with three rows of silk sutures is absolutely sure and can be best recommended. It is not more essential whether a duodenal stump thus fixed gets again sutured with the surrounding peritoneum. Of course the peritonealisation of the stump can be added by means of the remains of the small omentum or of gastrocolic ligament.

In cases of duodenal ulcer with shrinking of the duodenum, where we have to be especially economical with the available duodenal wall, it is best, to close the stump by the open duodenum without applying the Payr's forceps. The duodenum is then after the application of two holding threads and the Brunner's clamp either by means of a knife or with the electric loop cut in two under this clamp and the open duodenal stump is held free by the assistant at these two holding threads. Previous to that, the duodenum has been tightly covered with clothes as usual. This gives also a nice chance to look for ulcers in the open duodenum. The very little quantity of duodenal content, which may be discharged from the open duodenum at this procedure, cannot be of great disturbance for the surgeon. First of all the duodenal mucous membrane is closed by means of a noninterrupted catgut suture and then by two other rows as described before.

Cutting of the mesocolon window, and searching for the first jejunum loop—The transverse colon is lifted from the abdomen and its mesocolon expanded. Leftwards from the stock of the middle colic artery an incision is made within that place of the mesocolon which is poor in vessels in the length of about 5-6 cm. The opening in the mesocolon reaches from the mesenteric root close upto the insertion of the mesocolon in the colon.

The following procedure leads quickly and surely to get at the first jejunum loop: After lifting the transverse colon up from the abdominal cavity, the right hand of the surgeon goes into the abdominal cavity and palpates along the vertebral column. The hand then slides leftwards from the vertebral column into the depth without losing contact with the transverse mesocolon and is now on a place, where the finger hits a loop of the small intestine. Just that is the first jejunum loop, which may also be very easily recognized, for being fastened to the posterior wall of the abdomen by the plica duodenojejunalis and cannot be drawn up from the depth like other loops of the small intestine.

Preparation for applying the stomach-jejunum anastomosis—The first jejunum loop is drawn through the window of the transverse mesocolon and the loop is grasped into a straight

and elastic intestinal clamp according to Kocher, at a distance of about 5-6 cm. from the plica duodenojejunalis. The Kocher's clamp is just a modification of the originally soft intestinal clamp by Doyen, who has to be given credit for introducing soft elastic clamps to the gastric and intestinal surgery. The knotted intestinal clamp according to Graser is now applied at the stomach right at that place, up to a point where the small omentum and the gastrocolic ligament has been previously loosened from the stomach. The left edge of the incision of the mesocolon window is now sutured to the stomach below the Grasser's clamp by means of a few interrupted silk sutures. This row of suture is covered with folded gauze and both the clamps are placed, parallel to each other. If we most likely choose the first jejunum loop for the anastomosis, we must in spite of that, take much care, not to cause any kinking of the intestine, due to a too strong tension, when we suture the jejunum to the stomach in the region of the plica duodenojejunalis. When applying the jejunum to the stomach the end of the jejunum loop directed towards the duodenum chosen for the anastomosis is joined to the small curvature of the stomach the other end of the jejunum loop directed aboralwards lies by the large curvature. Both the ends of the jejunum loop, which lie in the clamp, are sutured to the small-resp. Large curvature of the stomach by means of two holding threads and on both these holding threads are put clamp forceps with sliding catch. Thus, both the organs, the stomach as well as the jejunum are unmovably connected to each other, a situation, which may not even always be reached by both clamps, for they are liable to move or may even get loose. It is also not always possible to avoid this unfavourable event even, if one tries the free arms of the clamp with a little thread. Finally a second small curved intestinal clamp is applied according to Hansy, 2-3 cm. above the Graser's knotted intestinal clamp. Now that part of the stomach, which lies between those two clamps is cleaned of its content. Later, after applying the anastomosis, the stomach is resected above the knotted Graser's clamp; the curved Hansy's intestinal clamp remains at the resection preparation.

It is also very easily possible, to apply that portion of the jejunum loop, which has been chosen for the anastomosis to the stomach by means of the previously mentioned method and to fasten it with two holding threads without grasping into the Kocher's clamp previously. In this case only two clamps lie at the stomach during the finishing of the anastomosis but none on the jejunum.

The place of the anastomosis including the clamps and the holding thread is most carefully covered with four clothes in such a way, that only the two organic parts of the stomach and of the jejunum, which are to be anastomosed to each other, are left free. Now one can begin with the anastomosis. It is applied according to the suggestion of Reichel and Polya as an end to side connection between the entire transverse incision of the stomach and of the jejunum.

Actual carrying out of the anastomosis—The anastomosis begins with a posterior lateral interrupted suture between the serosa of the stomach and of the jejunum, and is applied at the jejunum close to both the clamp (the knotted Graser's intestinal clamp at the stomach and the straight elastic clamp according to Kocher). The threads are cut up and only the two holding threads, which have been previously put on both the corners of the anastomosis, remain as a sign for the length of the posterior serous suture. Corresponding to the length of the anastomosis, the seromuscular coat of the stomach and of the jejunum is then longitudinally incised, without opening the mucosa of these organs. The inner edges of the incision of both the seromuscular incision are sutured with a straight needle (one generally is able to sew much quicker with a straight needle than with a curved one) by an uninterrupted round twisted suture, beginning at one corner of the anastomosis and finishing at the other. On both ends of this posterior and uninterrupted seromuscular suture are left long ends of thread which are also grasped into two clamp forceps with sliding catch. Now is the right moment to incise the mucous membrane of the stomach and of the jejunum, either with the knife, the scissors, with the electric loop, or with diathermy knife along that line, which has been chosen for the anastomosis. Thus the lumen of the stomach and of the jejunum has been opened, a procedure, which must be done very carefully, as to have enough chance to remove the content to the stomach and of the jujunum, either by sucking or by means of the tampon; thus the surrounding of the anastomosis is kept clean. The incision line of the mucous membrane of the stomach is now continued to the frontal wall of the stomach where the entire thickness of the wall of the stomach is cut. Those opening of the stomach and of the jejunum, ready for the anastomosis, are now next to each other. Before the suture of the mucous membrane is begun it is not needless, to open the two clamps somewhat, in order to stop bleeding which mostly comes from the subserous vessels. There is no danger for the anastomosis to be essentially displaced, when opening these two clamps, for at that time, the jejunum has been fixed to the stomach already by two rows of sutures. On the other hand there is now a chance to grasp the bleeding vessels of the subserosa and are to ligate them, a procedure, which avoids the postoperative after bleeding to a great extent.

The suture of the mucous membrane is likewise made as an uninterrupted, round twisted suture. Contrary to the other rows of suture, which are made with silk or thread, this last mentioned one is made with a catgut thread. In order to avoid, that all three rows of suture start at the same place, (we mean by that the corner of the anastomosis) the suture of the mucous membrane begins in the centre of the posterior circumference of the opening of the anastomosis. The catgut thread is right at this place tied in and the posterior margins of the mucous membrane of the stomach and of the jejunum are sutured towards the large curvature with a straight needle. When the corner of the anastomosis (corresponding to the large curvature) is reached the corner suture is done and that on the stomach by stitching the thread out from inside to outside and at the jejunum by putting the thread from outside to inside. Thus the thread reaches the frontal margin of the mucous membrane of the stomach and of the jejunum and sutures them together with an uninterrupted round twisted suture up to about the centre of the frontal circumference of the anastomosis, where the end of the thread remains after making a knot. With a second catgut thread, which is twisted on at the end of the first catgut thread right in the centre of the posterior circumference of the anastomosis, the posterior margins of the mucous membrane are likewise sutured towards the small curvature.

After making the corner suture, corresponding to the small curvature by stitching the thread out at the stomach from inside to outside and setting the thread at the jejunum from outside to inside, the frontal edges of the mucous membrane are connected with each other up to the centre of the frontal circumference of the anastomosis; the end of the thread is knotted now with the remaining end of the first catgut thread and then cut up. This finishes the suture of the mucous membrane, and the lumina of the stomach and of the jejunum are closed. This uninterrupted round twisted suture of the mucous membrane has the advantage that it reduces the bleedings of the mucous membrane. The technique is not essentially changed, if the uninterrupted catgut suture of the mucous membrane begins similar to all other rows of sutures at the corner of the anastomosis. Also the incision margins of the mucous membrane can be joined by uninterrupted catgut sutures. If it should occur during the applying of the suture of the mucous membrane, that the margins of the mucous membrane at the stomach is longer than the edge of the mucous membrane at the jejunum, then we are easily able to equalize them, by laying the mucous membrane of the stomach in folds several times and then finish the suture.

After finishing the suture of the mucous membrane, the surgeon as well as the assistant clean their hands most carefully and the frontal seromuscular suture follows in the usual way as uninterrupted round twisted suture with silk or thread. The beginning and also the end of the thread are knotted with the remaining ends of the posterior seromuscular sutures, which are fastened at the clamp forceps with sliding catch. The clamps, the knotted intestinal clamps according to Graser, which lies at the stump of the stomach and the straight clamp according to Kocher which clasps at the jejunum are now removed, as also the gauze applied under the anastomosis. The frontal seromuscular suture is covered by a frontal Lembert's serosa suture in form of a silk or thread interrupted suture. Both the corners of the anastomosis may possibly be oversutured each by a serosa suture. This finishes also the anastomosis completely.

Care of the stomach jejunum corner and closure of mesocolon window: Finishing of the operation—The angle between the stomach and the jejunum corresponding to the small curvature, (right at this place there is a possibility of an untight suture) is in so far made safe, as one sutures here an end from the small omentum to these organs. This end was previously created by the ligature and separation of the small omentum from the small curvature, and marked by leaving the thread of the ligature long and putting them into the clamp forceps with sliding catch. This end of the small omentum is put into the angle between the stomach and the jejunum and fastened to both these organs by several sutures as some kind of an omentum plug.

Next to that, the right edge of incision of the mesocolon window is sutured to the frontal wall of the stomach a little above the anastomosis by means of several interrupted sutures, while the left margin's incision of the mesocolon window has already been brought into connection with the posterior wall of the stomach previous to the beginning of the anastomosis. Thus the mesocolon window is closed; the stomach jejunum anastomosis lies now below mesocolon transversum. Before the laparatomy wound is closed in layers, the abdomen is most carefully looked into, specially the duodenal stump as well as the descending jejunum loop and one must be sure that all hæmorrhages have stopped. When closing the laparotomy wound, the parietal peritoneum is sutured with interrupted silk sutures; the very same is done with the fascia of the linea alba. The subcutaneous adipose tissue is sutured by interrupted catgut sutures, the skin is joined either by interrupted silk suture or by means of Michel's clamps.

The anterior anastomosis of the transverse colon—In those cases, where the transverse mesocolon is shortened to such an extent, (may be due to coalesces in cases of gastric or duodenal ulcers or by penetration of the carcinoma into the mesocolon) that we are unable to make a broad mesocolon window, which again creates the great danger of pinching of the descending jejunum loop by the too tight mesocolon fissure, the connection of the stump of the stomach with the jejunum is made anterior of the transverse colon in the already described way. In order to prevent a kinking of the transverse colon by the jejunum, that place of the jejunum, which is about 30-40 cm. below the plica duodenojejunalis is chosen for anastomosis. This enteroanastomosis is done, by applying short, curved intestinal clamps according to Doyen or according to Kocher to both the loops of the jejunum. One is able to make the very same connection just as safe, without using the clamps. The anastomosis is further sutured in three layers according to the same technique as has been used already at the application of the stomach jejunum anastomosis.

Some remarks about the resection for exclusion—The process of the resection for exclusion reminds essentially to the method Billroth II. In order to avoid a repetition of the technical part of the operation, only essential part is given below.

It seems to be of great importance to write something about the way of separating the stomach or the duodenum oralwards from the ulcer, because right there, most of the mistakes are made.

If the non-resectable ulcer of the duodenum is situated in the neighbourhood of the pylorus, then one excludes the ulcer by a transverse incision through the stomach oralwards from the pylorus. But in those cases, where one has to deal with non-resectable ulcers of the duodenum, which are placed in sufficient distance from the pylorus, the exclusion of the ulcer is obtained by a transverse separation of the duodenum right behind the pylorus.

The wall of the duodenum is often very much thickened and inflexible especially around a non-resectable ulcer, a fact, which compels one to separate the duodenum transversely further away from the oral edge of the ulcer, so as to enable one to turn the sufficiently long duodenal stump upside down and close it in three rows without any difficulty. The very same care and precaution must be used, when one has to exclude duodenal ulcer, placed near the pylorus. In a case like this, one must separate the stomach transversely at least 4 cm. before the pyloric spincter in order to be sure about the closing of the stump of the stomach. One gets great difficulties to close a pyloruswards placed stump of the stomach, if the stomach has been separated too near to the pylorus. Such a stump can-

not either be closed at all, or if so after all, there is the great danger, that the sutures loosen very soon.

METHOD BILLROTH I

Also this method starts with the exact and careful examination of the common bile duct, of the posterior wall of the stomach and of the duodenum from the omental bursa, similar to the method Billroth II. The ligature of the gastrocolic ligament and of the small omentum with the separation of the right and left gastric arteries is done corresponding to the entire pars præpylorica. Contrary to the method Billroth II. the preparation of the duodenum must be done very carefully and cautiously. One must give one's best attention to the nutrition of the wall of the duodenal stump, for this stump is brought into direct connection with the stomach. The duodenal stump may not be loosened in the method Billroth II far from its surrounding, but must remain in connection with the neighbourhood. Corresponding to that place, where the stomach should be separated, Hansy's clamp is applied at the stomach. In case of ulcer of the stomach the duodenum transverse is resected right behind the pylorus and in a case of a duodenal ulcer aboralwards from the ulcer and the duodenal stump is fastened to the stomach by means of two holding threads. The lower duodenal stump must be in one line with the large curvature of the stomach. The anastomosis between the stomach and the duodenum is applied by open duodenal stump, which means without pinching the duodenum. The posterior serosa of the stomach is connected with the posterior duodenal wall, corresponding to the breadth of the duodenum by means of a Lembert's interrupted silk suture. While the thread on both the ends of this row of the suture is left long and fastened to a clamp forceps with sliding catch, all the remaining ends of the thread are cut off. The posterior serosa of the stomach and the external layer of the posterior duodenal wall are longitudinally incised up to the mucosa of the stomach and of the duodenum and the inner margin of the incision of the seromuscularis is sutured either by means of an uninterrupted round twisted suture made of silk or by an interrupted suture; the ends of the threads of this row are also left long and the clamp forceps with sliding catch are put to them. When making this row the stitches are set at a little further distance on the wall of the stomach, while they must be tightly set at the duodenum. Now the mucous membrane of the stomach is opened corresponding to the place of the anastomosis, and at the same time the prepared part of the stomach is resected by transverse separation in the same line, as the incision of the mucous membrane had been previously made.

The lumina of the stomach and of the duodenum lie now parallel and the opening of the stomach is much broader than that of the duodenum. The margin of the mucous membrane of the stomach and of the duodenum of the posterior circumference of the anastomosis are joined, beginning at the side of the large curvature of the stomach by means of a catgut thread as uninterrupted round twisted suture. The stitches of the suture of the posterior mucous membrane at the mucosa of the stomach are in a little further distance as at the mucosa of the duodenum. Besides this, the mucous membrane of the stomach is folded several times, when applying the suture, while the margin of the mucous membrane of the duodneum is only simply grasped. Thus the mucous membrane tube of the stomach becomes still more raked and thus, more or less equalized the difference in the length of the transverse incision of both these organs. Now follows the uninterrupted suture of the mucous membrane of the frontal circumference of the anastomosis, a process, which closes the lumen of the stomach and of the duodenum. The next row of suture is the frontal seromuscularis suture also done as uninterrupted round twisted suture and finally the frontal serosa suture is applied as interrupted silk suture. Thus the probably left of culdesac form plus of the diameter of the stomach at the side of the small curvature of the stomach is removed by a turning upside down serosa suture and the place of the anastomosis of the stump of the stomach little by little turns into the duodenal stump, without leaving any step or mark to see. The application of some interrupted sutures close to the opening in the small omentum and in the ligamentum gastrocolicum finishes the operation.

SOME REMARKS ABOUT THE OPERATION OF THE JEJUNAL ULCER

In most of the cases of our clinic, where we have to make an operation on account of a relapsing jejunal ulcer, we operate according to the method Billroth II, and apply the connection between the stump of the stomach and the jejunum behind the transverse colon. According to that, the first and often very complicated task of the operation is the exhibition of the jejunal ulcer, which is covered by the transverse mesocolon as well as to free the stomach jejunum anastomosis out of the mesocolon fissure. Considerable difficulties may arise at this part of the operation due to widely extended coalesces. Much care and attention must be given to the vessels of the mesocolon, such as first of all the medial colic artery in order to prevent disturbances of nutrition of the transverse colon by injuring or ligaturing of the vessels.

As soon as the transverse colon with its mesocolon is loosened from the stomach jejunum anastomosis, a ligature is first applied to the mesentery of the jejunum loop, which has been previously used for the anastomosis with the stomach. It is cut in two and then the jejunum is separated at two places transversely; this the first time in the region of the ascending jejunum loop and the second time aboralwards from the jejunal ulcer in the course of the descending jejunum loop. At the ascending and descending jejunum loop right there, where the loops are to be cut through, two by two short and curved intestinal clamps are applied according to Doven or Kocher and the jejunum is separated between these clamps. After this two fold separation of the jejunum remains only one short piece of the jejunum connected with the stomach. This piece of the small intestine corresponds exactly to that place of the jejunum, which has prevoiusly been used for the anastomosis. Both the ends of this jejunum loop are closed by clamps and are besides covered with the gauze. The stomach plus the connected jejunum-loop are layed round before the laparotomy wound to the left.

Between the oral end of the ascending and the aboral end of the descending jejunum loop (the latter runs downwards within the mesocolon fissure and is now only a little drawn upwards) an end to end anastomosis is made; previously to that both the short and curved intestinal clamps are put according

to Doyen or according to Kocher, which lie on both the stumps of the jejunum parallel to each other. The anastomosis is done in the already well known way in three layers. Then follows the end to side anastomosis which one already is acquainted with from the method Billroth II between the entire transverse cut of the stomach and the jejunum. Thus the previously mentioned circular jejunum anastomosis gets to lie above this stomach jejunum connection. Before the jejunum is sutured with the posterior Lembert suture to the stomach, fasten the left edge of the mesocolon fissure can also be fastened first of all to the posterior wall of the stomach by means of interrupted sutures. A small part of the stomach is resected which lies above the old stomach jejunum anastomosis a short loop of the jejunum together with the ulcer is placed right there. The right margin of the mesocolon window is now sutured to the frontal wall of the stomach above the stomach jejunum anastomosis, and thus the mesocolon fissure gets closed, and the operation is finished. The final condition, which is produced by this procedure is very similar to the method Billroth II with a retrocolic placed anastomosis between the stomach and the jejunum.

Some times it happens, that in cases of ulcers pepticum jejuni with a retrocolic lying stomach jejunum connection, the ulcer breaks deeply in, either into the mesocolon transversum or into the colon transversum. If such is the case, a piece of the colon transversum is resected very frequently; and this resected piece remains at the other resection preparation. Both the stumps of the colon are connected end to end in three layers according to the usual technique after the other operation has been finished at the jejunum and at the stomach previously.

In such cases of ulcus pepticum jejuni, which have developed in spite of resecting the first ulcer according to the method Billroth II with an anticolic placed stomach jejunum connection and continuing entero anastomosis according to Braun, we are able to find the place of the ulcer mostly soon after the opening of the abdominal cavity, for it is not covered by the colon, resp. by the mesocolon transversum. In this case, the lossening of the stomach jejunum anastomosis from the mesocolon fissure is not necessary. The operation is limited to the removal of that ulcer containing part of the jejunum, which has been previously connected with the stump of the stomach by the anastomosis and further to the resection of a small piece of the stomach above the old stomach jejunum anastomosis. The resection begins with the ligature and separation of that part of the mesentery which belongs to the ulcerated jejunum loop. When this is done, the jejunum is separated at the ascending and descending peduncle and the ulcerated piece of the jejunum is resected. The oral stump of the ascending and the aboral stump of the descending jejunum loop are connected by means of a circular anastomosis in three rows and a new connection between the stumps of the stomach and of the jejunum, end to side, is applied. Thus the new stomach jejunum anastomosis lies below the previously mentioned end to end anastomosis of the jejunum. As a rule, the Braun's entero anastomosis, which has been applied at the first operation can be saved at this time and one is able to use it at the second operation. This proves to be right especially in those cases, where one has selected a sufficient long anticolic placed jejunum loop at the first operation.

In consideration of the technical difficulties, which may arise when resecting an ulcus pepticum jejuni, it would be advisable to think about a more frequent use of the method Billroth II, with an anticolic lying stomach jejunum anastomosis following Braun's entero anastomosis at the first removement of a chronic stomach or duodenal ulcer.

Re-examination about Permanent Results after Gastric Resection for Gastric and Duodenal Ulcers

The first Billroth's method was only used in ulcus ventriculi in one-third of the cases, and in ulcus duodeni only in 2·6 per cent. The resection for exclusion was used in cases of ulcus duodeni and that in 6·3 per cent. The simple gastro-entero anastomosis was only applied in 3·3 per cent of all cases.

Mortality of the Resection

The mortality in cases of ulcus ventriculi and duodeni are 3·3 per cent. In cases of perforated ulcus ventriculi and duodeni the mortality of resection amounts to 5·5 per cent.

Permanent Results

The operated patient does not completely digest all kinds of food as indigestible farinaceous food, pulses, beans, peas etc., and he complains about pyrosis after fatty food. These symptoms were found in 4·1 per cent and that, after operating according to Billroth II method. The healing has been obtained in 95·9 per cent of the cases. Very frequently it is observed that the patient after resection operation was neither able to digest milk nor light coffee.

Gradually to the increasing experience, the mortality rate will no doubt become reduced. Of great support to that aim will also be the more frequent use of splanchnic anæsthesia instead of the ether narcosis and further, in cases of duodenal ulcers, which are difficult to resect, the more frequent use of the resection for exclusion. In cases of perforated ulcers cases should be carefully selected for resection and for patients, where the general condition is not very favourable and 7 to 12 hours have passed since the perforation it is much better to use the covering suture of the perforation's lacuna instead of the resection, but without applying a gastroentero anastomosis, for this would be of great danger in an ulcus pepticum jejuni.*

* Read at the U. P. Provincial Medical Conference held at Benares in December 1941.

NOTES AND NEWS

INDIAN MEDICAL SERVICE

As a wartime measure, the Government of India have decided that medical practitioners who hold the following qualifications will be eligible for appointment to the Emergency Cadre of the Indian Medical Service:

1. Bachelor of Medicine and Bachelor of Surgery of the Mysore University. (M.B.B.S., Mysore.).
2. Bachelor of Medicine and Bachelor of Surgery of the Osmania University. (M.B.B.S., Osmania.).

Indians holding foreign dental qualifications will be admitted for recruitment to the Dental Branch of the Indian Medical Service (Emergency Commission). Each case will be considered on its merits by the Selection Board.

Candidates selected for Emergency Commission in the Indian Medical Service for duty within Indian limits may be granted an advance of pay not exceeding Rs. 300/- at the time of appointment. The advance will be recovered by monthly instalments of one-third of his pay.

BHALCHANDRA KRISHNA MEMORIAL FUND GOLD MEDAL

At a meting of the subscribers of Sir Bhalchandra Krishna, Kt., Memorial Fund held on the 11th July, 1942, the following resolution was adopted:

"That from the funds collected to perpetuate the memory of the late Sir Bhalchandra Krishna, Kt., a Memorial Prize Medal be founded to be awarded every year on the anniversery of his death to a member of the medical profession who submits a thesis or delivers a lecture on any medical subject before a meeting of the medical profession to be held under the auspices of the Bombay Medical Union, preference to be given to one who submits any original or research work especially with reference to Indigenous Medicine on Western lines."

In consequence with the above resolution, members of the profession are invited to submit a thesis or a paper by the 30th March, 1943, to the Jt. Hony. Secretaries, Bombay Medical Union for submission to a Selection Committee for making the above award.

The thesis or paper shall have to be read by the prize man on the day of the award at a meeting of the profession to be held in accordance with the above resolution.

MEDICAL RELIEF TO CYCLONE-STRICKEN AREAS

The members of the medical profession, under the auspices of the Bengal Provincial Branch of the Indian Medical Association, at a recent meeting formed a Working Commitee to organise and conduct medical relief in the cyclone-stricken areas. The committee consists of Dr. K. S. Ray (President), Dr. P. Chatterjee, Dr. Subodh Dutt, Dr. A. K. Ukil, Lt.-Col. J. C. De, the Director of Public Health, Dr. P. K. Guha, Dr. B. Banerjee, Dr. Sunil Dutta, Dr. M. U. Ahmed, Dr. A. D. Mukharji, Major P. Bardhan, Dr. Subodh Mitra (members), Dr. A. K. Bose (treasurer), Dr. K. K. Sen Gupta and Dr. Suresh Dutta (Secretaries).

The working committee has already enlisted more than 100 senior medical students and a panel of doctors from different schools and colleges, to proceed to the affected areas to work in co-ordination with any official or non-official organisation already working in these areas.

It would facilitate the work of the committee if various organisations willing to avail themselves of the services of these medical volunteers communicate with the Secretaries of the committee at 67, Dharamtalla Street, who will furnish all necessary information at the office between 6 p.m. and 8 p.m., 'phone Cal. 1570.

Medical men, students or doctors, willing to volunteer their services are requested to send their names to the Secretaries—*A.P.*

VEGETABLE INSECTICIDES IN INDIA

The discovery of several useful vegetable insecticides and the possibilities of their cultivation in India are revealed in a leaflet (No. 220) just published by the Forest Research Institute, Dehra Dun.

For controlling agricultural as well as household pests vegetable insecticides are preferred to others, such as lead and copper salts, arsenic and nicotine, because they are non-poisonous to man and animals.

The growing demand for vegetable insecticides was hitherto met mainly by a plant called 'derris' from Malaya, Dutch East Indies and Philippines. Investigations conducted by the Forest Research Institute have now shown that other plants bearing the same toxic content as 'derris' are available in this country; and the existing materials are rich enough for the preparation of effective insecticidal emulsions and powders. Their toxic content is capable of still further improvement by proper cultivation and treatment. Certain parts of India, it has been found, possess suitable climatic and soil conditions for the introduction and cultivation of richer varieties of Malayan 'derris'. Experiments in this direction have already proved successful in Mysore, Cochin and Assam.

VITAMIN PRODUCTION IN THE SOVIET UNION

The Soviet Union has been one of the first countries to produce vitamins in a mass scale and distribute them to the people. During the present war, the production of vitamin concentrates has been greatly stimulated. It is now reported from Frunze that a vitamin C factory has been constructed there, the output of which is expected to be twice as big as the whole Soviet output of vitamin C concentrates before the war. The concentrate is produced from green walnuts, which are available in inexhaustible quantities in Kirghizia's rich forests—*Science & Culture.*

INTERNATIONAL ROLE OF SCIENCE

If we are to have a durable peace after the war, if out of the wreckage of the present a new kind of co-operative life is to be built on a global scale, the part that science and advancing knowledge will play must not be overlooked. For although wars and economic rivalries may for longer or shorter periods isolate nations and split them up into separate units, the process is never complete because the intellectual life of the world, as far as science and learning are concerned, is definitely internationalized, and whether we wish it or not an indelible pattern of unity has been woven into the society of mankind.

(*Continued at foot of next page first column*)

BOOK REVIEW

THE NATURAL DEVELOPMENT OF THE CHILD—By Agatha H. Bowley, 1942. Pages xvii+172. Crown 8 vo. With 84 photographic illustrations. Published by E. & S. Livingstone, 16 & 17 Teviot Place, Edinburgh.

A child grows in three ways—physically, intellectually and emotionally, that is, in character and personality. The first two have been extensively studied and we can gauge the development from time to time. The last one has been neglected too long and in this book the author has fulfilled a long want. Written in a simple language and avoiding technicalities as far as possible, this book will be highly interesting and instructive to parents, teachers and doctors. It will be a revelation to many who still advocate 'spare the rod and spoil the child' policy in this country, when they find that many difficult problems in a child may be tackled in a humane way. The subject is far from easy, mainly because there are no exact methods of measurements and comparison and where the individual differences are enormous. Progress in growth and intelligence can be almost accurately measured but in the development of personality the knowledge is apt to be a strange mixture of personal experience, memories and prejudice—confused by superstition, folklore and profitless moralising. Why a child when at 2 years has tantrums, at three he is troublesome about food, at seven he is a little defiant and unruly or at fourteen he is moody and reticent? After patient observation and enlightened deductions the writer has given a broad outline of psychological knowledge, which will help the parents teachers and doctors to deal with these difficulties more wisely.

The journey from babyhood to adolescence is an uphill and downhill task, with its smoothness and difficulties but it is an interesting one, full of adventures and challenging experiences. In the eight chapters the author has shown how this journey can be made not too difficult and the child can go through it with a healthy body and mind.

Chapter seven deals with the subject of "Children and the War." Since Dr. Mons (Air raids and the Child, *Brit. M. J.*, 1941, p. 625) quoted cases of children suffering from a lack of concentration and who were showing difficult, aggressive or nervous traits due to the effect of "being bombed" much controversy and interest were aroused. It was later shown by Dr. Burbury (Effects of Evacuation and Airraids on City Children, *Brit. M. J.*, 1941, p. 660) and others that in about 5 per cent new symptoms had arisen due to air raids and in 17 per cent symptoms were attributed to evacuation. The book contains the following leaflet approved by the Ministry of Information, England, which I suppose will be helpful to many parents in our country at the moment:

CHILDREN AND AIR RAIDS. SOME ADVICE TO PARENTS

Children imitate adults—If you show that you are afraid, children will show it too. Talk quietly and gently and expect them to do the same.

Children depend on adults—Try to be calm and to keep your head in the event of danger. You will have practised what to do in an emergency—so tell children what to do, and let them feel that they can leave the responsibility to you.

Children rely on adult approval—Tell them they are "civilian soldiers," and that you expect them to behave as such. Be strict about reckless behaviour.

Most children have a vivid imagination—Don't feed the imagination with bomb stories and premonitions of possible disaster. Talk about the bravery and efficiency of our defence services or better still, don't talk about the war at all. Just gossip of other things.

Children need occupation during air raids—Let them play and chatter normally. Try to think of songs and games to play with them, if they cannot amuse themselves.

Children need to be comfortable during air raids—See that they are warm. Give them something hot to drink, and some sweets to eat. If they are sleepy, let them sleep as comfortably as possible.

Children need to feel as secure as possible during air raids. If they *feel* it is safer to go out to a shelter, even although you would just as soon stay in the house, take them out.

If your child shows signs of being frightened—Do not shame him. Don't get angry with him. Talk calmly and confidently to him. Tell him that Hitler is trying to make him frightened with his noisy bombs and his silly old threats, and that it would only be helping him to win to let him succeed in his way. Teach your child to say "Boo" to Hitler. If a child becomes hysterical, take him away from the others, sponge his face and the back of his neck with cold water. Hold him tightly and soothe him.

A leaflet of this nature with slight alterations may be profitably printed in all newspapers and distributed to parents in this country when the enemy is at the door. But imagination, intelligence and patience are needed to appreciate fully the difficulties and apprehensions of the civilian population and official bodies in this country do not possess these attributes.

B. P. NEOGY.

(Continued from previous page)

There is not an area of activity in which this cannot be illustrated. An American soldier wounded on a battlefield in the Far East owes his life to the Japanese scientist, Kitasato, who isolated the bacillus of tetanus. A Russian soldier saved by a blood transfusion is indebted to Landsteiner, an Austrian. A German soldier is shielded from typhoid fever with the help of a Russian, Metchnikoff. A Dutch marine in the East Indies is protected from malaria because of the experiments of an Italian, Grassi; while a British aviator in North Africa escapes death from surgical infection because a Frenchman, Pasteur, and a German, Koch, elaborated a new technique.

In peace as in war we are all of us the beneficiaries of contributions to knowledge made by every nation in the world. Our children are guarded from diphtheria by what a Japanese and a German did; they are protected from small pox by an Englishman's work; they are saved from rabies because of a Frenchman; they are cured of a pellagra through the researches of an Austrian. From birth to death they are surrounded by an invisible host—the spirits of men who never thought in terms of flags or boundary lines and who never served a lesser loyalty than the welfare of mankind The best that every individual or group—has produced anywhere in the world has always been available to serve the race of men, regardless of nation or colour—*Rockefeller Foundation Review for 1941.*

CORRESPONDENCE

The Editor is not responsible for any views expressed by contributors

THE EDITOR, *Journal of the I. M. A.*, Calcutta.

THE USE OF COTTON AND SILK THREADS FOR SUTURES

Sir,

With reference to the article on "The use of cotton and silk threads for sutures" in your issue of August, 1942, it might be of some interest to the authors and to the readers to know that I in collaboration with Dr. T. S. S. Rajan, M.R.C.S., L.R.C.P., (under whom I have been working) have been using silk and cotton exclusively as our suturing materials for the past 17 years. From our experience of over 1,000 major operations and many more of minor operations, I could say we have never found the necessity of changing these, our suturing materials

I have used both plaited and twisted varieties of silk sutures of moderate thickness (size 1 to 3). After the beginning of the present war, I have found it rather difficult to get the required size of sutures from the companies. And so I am now having my silk ligatures twisted by the local silk weavers. And this variety of sutures are much cheaper than the company-made ones, serves the purpose very well and stands boiling without untwisting.

The usual type of cotton thread used by me is the ordinary sewing thread in wooden reels, size between 30 to 50, bought locally from the bazars.

These silk and cotton threads are cut in lengths just longer than what is required for an ordinary ligature and made into wide easy loops or they are separately rolled, loosely over a perforated spool (glass preferable) in sufficient lengths. These loops and spools are boiled for an hour and kept in sterilised containers for emergency use. For every operation, the necessary quantity of cut cotton and silk threads made into the form of loops or spools are boiled along with the surgical instruments in a separate ladle.

I use silk for all intraperitoneal and peritoneal sutures (thin size) except to ligature small vessels in these regions or omentum where I use cotton threads. Cotton is used in all extraperitoneal regions except in places where there is a likelihood of some tensions on the sutures. In those places thin silk is used. I have found no ill-effect resulting from the interchanging of these two materials.

My general observations on the use of these suturing materials are:—

1. Easy and fine approximation without much tension on the tissues. 2. They stand boiling very well. 3. They are very cheap and easily available. 4. Of course, there were stray cases of sepsis which required the removal of the suture for the closing of the wound. This is easily done by fishing out the stitch with a sinus forceps through the existing opening. 5. Cotton is preferable in septic cavities, in places where there are chances of sepsis and in places where there are chances of contamination of urine or vaginal discharge, etc. I am, etc.,

Rajan Clinic
Trichy, Madras
28-9-42.

P. E. JAMBUNATHAN,
L.M. & S.

L. M. P. COURSE IN THE STATE MEDICAL FACULTY OF BOMBAY

Sir,

I thank you very much for sending me a copy of Dr. Narayan Rao's letter which is a rejoinder to my communication on L. M. P. (Bom.) published in the October issue of the Journal of the Indian Medical Association.

Analysing Dr. Narayan Rao's vituperations expressed in the language more suited to a lay press than to the columns of an organ of a Scientific Association, I find that he desires to say the following:—

(1) That he and his Licentiates do not want to establish step by step a uniform standard of medical education as laid down by the Medical Council of India. They must have it at one stroke.

(2) Unless they have it at one stroke, he will prefer to keep all the present and future students in medical schools as inferior medical men. The Bombay Government has assured him that Ahmedabad and Poona Schools would be converted to medical colleges before long.

(3) Possessed with the above convictions, he has welcomed the move of the Government of Bombay in instituting the L. M. P. diploma, which will be given after 3½ years study.

(4) That the increase of L. C. P. S. Course to 4½ years from 3½ years is solely due to three Mehtas in the Council.

(5) That I as an office-bearer of the I. M. A. which had passed a resolution No. 14 of the 15th All-India Medical Conference should not have associated with the gradual process of securing a uniform standard of medical education in the Medical Schools in Bombay.

Now Sir, the resolution referred to by Dr. Narayan Rao requests the *Provincial Governments* to take early steps to establish a uniform minimum standard of medical education in their respective Provinces, the standard being that of University degree and to abolish all examining bodies other than the Universities which may be granting medical deplomas and licenses.

When the resolution is read in its true spirit it recommends first to take steps to establish uniform standard of training in the medical schools and when such a standard is established, to abolish the Examining Bodies other than the University.

If one reads my letter published in the last issue of the Journal one will find out what genuine efforts the College of Physicians & Surgeons, Bombay, has made to force the authorities of the Medical Schools in Bombay Province to bring the standard of medical education to a uniform standard.

It raised the preliminary education standard for admission to Medical Schools to Inter Science sometime ago. It now extended the period of clinical study to three years as required by the Medical Council of India. They could not increase the

period of Preclinical study to 2 years from 1½ years because the Government would not equip the laboratories and engage staff sufficient and efficient as required to teach the Preclinical subjects satisfactorily, in spite of repeatedly bringing it to the notice of the Government.

It can thus be seen that the College is seriously trying to bring the course of L.C.P.S. (Bom.) to the standard required by the Medical Council of India.

It has been found not possible to raise the course to the uniform standard at one stroke as the Government of Bombay would not co-operate with the efforts of the College.

It's only Madras which converted at one stroke one of their Schools into a College and closed down the rest. One gives the Madras Government credit for this conversion, but one would prefer to convert all the Schools into Colleges step by step rather than raising one at one stroke and closing down the rest.

Besides Madras, Bombay College of Physicians & Surgeons is the only body in the country which is actively and honestly trying to comply with the recommendations of the Delhi Conference and the members of the Indian Medical Association who are on the Council of the College contribute a great deal towards this effort of the College.

I honestly fail to understand Dr. Narayan Rao's reasoning justifying him to welcome the Bombay Government's move to institute a State Medical Faculty and a L.M.P. Diploma of 3½ years training and his accepting a seat on the Board of that Faculty. Does he act thereby in conformity of his Association's mandate which is, as he says, "End it or mend it completely"? He is certainly not able to mend it yet and his action in accepting a seat on the Board of newly established Faculty does not prove his intention to end it.

Does he honestly believe that the Bombay Government intends to convert the Schools under their management into Colleges before long? The Government repeatedly assured the College during the past number of years to improve the equipment and staff to raise the standard of training and once even promised to convert the Schools into Colleges and to stop admissions to L.C.P.S. Course from a fixed date. Has the Government kept any of those promises? What guarantee has Dr. Narayan Rao got from the said Government to be so sure as to its fulfilment? If they really wanted to convert their Schools into Colleges before long they would not have gone to the extent of establishing State Medical Faculty with a special Board of its own and institute a special diploma. This is a definite plan to work up to a policy of perpetuating an inferior qualification in the Bombay Province. To those who have read the present Surgeon General with Government of Bombay Major General Candy's views as expressed at the Delhi Conference, the action of the Government, whose expert adviser in matters medical he is, makes its intentions quite clear.

A seat on the Board of the State Medical Faculty should not blind an eagle eye of a strong champion of the Licentiate's rights like Dr. Narayan Rao.

I hope he will study the action of the College dispassionately, getting himself free of his personal prejudices against the College and its individual members and not misguide the Licentiates.

It's the most retrograde step the Government of Bombay has taken and the College of Physicians & Surgeons, Bombay, is fighting against it.

I do not think I am guilty of any breach of discipline or want of faithfulness to the Association on the score of being one of its office bearers, by my supporting the action of the College of Physicians & Surgeons, Bombay, which is endeavouring to implement the resolution of the Indian Medical Association referred to by Dr. Narayan Rao.

I do not think it worth my while to reply to Dr. Narayan Rao's remarks against the "Mehta trio" as every one knows that the Council of the College of Physicians & Surgeons, Bombay, consists of 22 members, most of whom are experienced, hard tried and eminent persons of the medical profession; Mehtas are only three.

I request the Indian Medical Association and the All-India Licentiates Association to take up this matter seriously and study the question as soon as possible before the newly established State Medical Faculty grafts itself permanently on the soil of Bombay Province. I am, etc.

CHAMANLAL MEHTA

Bombay, 31-10-42.

It is regretted that it will not be possible to publish any more correspondence on this subject—EDITOR, *J.I.M.A.*

IX U. P. PROVINCIAL MEDICAL CONFERENCE

POSTPONED

Dr. J. W. Phillips of Gorakhpur, Organising Secretary, U. P. Provincial Medical Conference regrets to announce that the Conference has been postponed till October, 1943, in compliance with the suggestion of the Annual Provincial Council Meeting held at Lucknow on October 24, 1942.